* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	18	FEB 10	STN Patent Forums to be held in March 2005
NEWS	19	FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005
NEWS	20	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	21	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	22	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23	MAR 02	GBFULL: New full-text patent database on STN
NEWS	24	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:44:41 ON 03 MAR 2005

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=> file reg
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'REGISTRY' ENTERED AT 14:44:50 ON 03 MAR 2005
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STRUCTURE FILE UPDATES:    2 MAR 2005  HIGHEST RN 841200-41-7
DICTIONARY FILE UPDATES:   2 MAR 2005  HIGHEST RN 841200-41-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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Experimental and calculated property data are now available. For more
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to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\09854694.str
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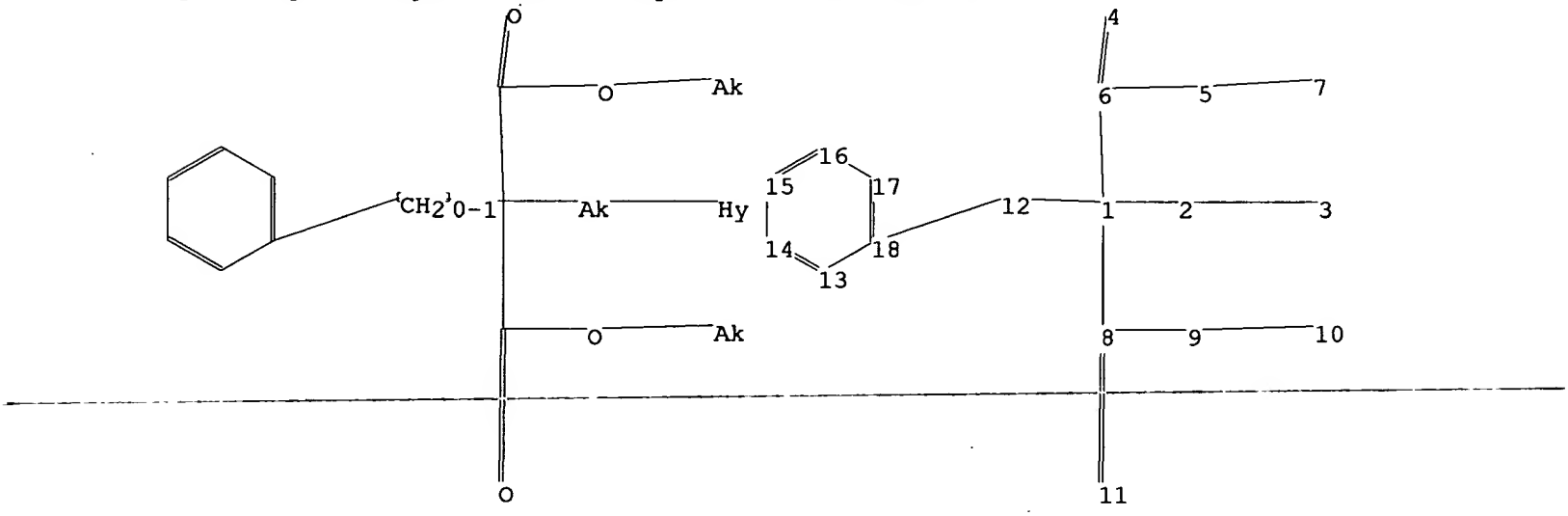


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chain nodes :
1  2  3  4  5  6  7  8  9  10  11  12
ring nodes :
13  14  15  16  17  18
chain bonds :
1-2  1-6  1-8  1-12  2-3  4-6  5-6  5-7  8-9  8-11  9-10  12-18
ring bonds :
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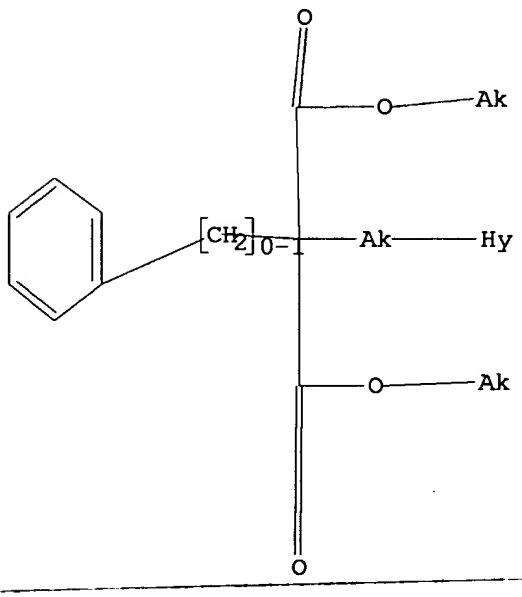
13-14 13-18 14-15 15-16 16-17 17-18
exact/norm bonds :
1-2 2-3 4-6 5-6 5-7 8-9 8-11 9-10
exact bonds :
1-6 1-8 1-12 12-18
normalized bonds :
13-14 13-18 14-15 15-16 16-17 17-18

Match level :
1:CLASS 2:CLASS 3:Atom 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom
Generic attributes :
3:
Saturation : Unsaturated

L1 STRUCTURE UPLOADED

=> dis l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 9934 TO ITERATE

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

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                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       192708 TO   204652
PROJECTED ANSWERS:             130 TO      664

L2            2 SEA SSS SAM L1

=> s l1 full
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FULL SCREEN SEARCH COMPLETED - 192928 TO ITERATE

100.0% PROCESSED  192928 ITERATIONS                          201 ANSWERS
SEARCH TIME: 00.00.12

L3          201 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   161.33     161.54

FILE 'CAPLUS' ENTERED AT 14:45:41 ON 03 MAR 2005
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 3 Mar 2005  VOL 142 ISS 10
FILE LAST UPDATED: 2 Mar 2005  (20050302/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

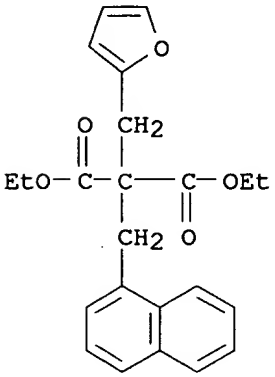

=> s l3
L4            96 L3

=> s l4 and pd<dec 1998
      18918148 PD<DEC 1998
                    (PD<19981200)
L5            79 L4 AND PD<DEC 1998

=> dis l5 1-79 bib abs hitstr

L5   ANSWER 1 OF 79  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   1999:104651  CAPLUS
DN   130:139217
TI   New synthesis of diethyl (1-naphthylmethyl)tetrahydrofurfurylmalonate
AU   Zhou, Zhi-Ming; Chen, Nan
```

CS College of Chemical Engineering & Material Science, Beijing Institute of Technology, Beijing, 100081, Peop. Rep. China
SO Gaodeng Xuexiao Huaxue Xuebao (**1998**), 19(12), 1979-1981
CODEN: KTHPDM; ISSN: 0251-0790
PB Gaodeng Jiaoyu Chubanshe
DT Journal
LA Chinese
AB The title compound was prepared in 3 steps from furfural and di-Et malonate via alkylation of di-Et tetrahydrofurfurylmalonate with 1-(chloromethyl)naphthalene in DMF in the presence of NaH.
IT **95432-29-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of di-Et (1-naphthylmethyl)tetrahydrofurfurylmalonate)
RN 95432-29-4 CAPLUS
CN Propanedioic acid, (2-furanylmethyl)(1-naphthalenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



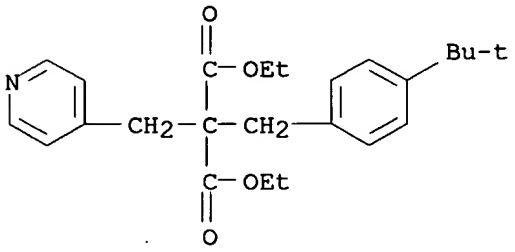
L5 ANSWER 2 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:492785 CAPLUS
DN 129:227381
TI Specificity of pyridinium inhibitors of the ubiquinone reduction sites in mitochondrial complex I
AU Miyoshi, Hideto; Iwata, Jun; Sakamoto, Kimitoshi; Furukawa, Hiroshi; Takada, Motoyuki; Iwamura, Hajime; Watanabe, Takashi; Kodama, Yoshio
CS Division of Applied Life Sciences, Graduate School of Agriculture, Kyoto University, Kyoto, 606-8502, Japan
SO Journal of Biological Chemistry (**1998**), 273(28), 17368-17374
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
OS CASREACT 129:227381
AB Dual binding sites for pyridinium-type inhibitors in bovine heart mitochondrial complex I have been proposed (Gluck, M. R., Krueger, M. J., Ramsay, R. R., Sablin, S. O., Singer, T. P., and Nicklas, W. J. (1994) J. Biol. Chemical 269, 3167-3174). The marked biphasic nature of the dose-response curve for inhibition of the enzyme by MP-6(N-methyl-4-[2-(p-tert-butylbenzyl)propyl]-pyridinium) makes this compound the first selective inhibitor of the two sites (Miyoshi, H., Inoue, M., Okamoto, S., Ohshima, M., Sakamoto, K., and Iwamura, H. (1997) J. Biol. Chemical 272, 16176-16183). Modifications of the structure of MP-6 show that a tert-Bu group on the

benzene ring, a Me group attached to the pyridine nitrogen atom, para-substitution pattern in the pyridine ring, and the presence of a branched structure in the spacer moiety are important for the selective inhibition. On the basis of the structural specificity, we synthesized a selective inhibitor, MP-24 (N-methyl-4-[2-methyl-2-(p-tert-butylbenzyl)propyl]pyridinium), which elicits greater selectivity. Characterization of the inhibitory behavior of MP-24 provided further strong evidence for the dual binding sites model.

IT **212787-47-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyridinium inhibitors of ubiquinone reduction sites in mitochondrial complex I)

RN 212787-47-8 CAPLUS

CN Propanedioic acid, [[4-(1,1-dimethylethyl)phenyl]methyl](4-pyridinylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:686572 CAPLUS

DN 128:22692

TI Potential GABAB receptor antagonists. X. The synthesis of further analogs of baclofen, phaclofen and saclofen

AU Prager, Rolf H.; Schafer, Karl

CS Department of Chemistry, Flinders University of South Australia, Adelaide, S.A. 5001, Australia

SO Australian Journal of Chemistry (**1997**), 50(8), 813-823
CODEN: AJCHAS; ISSN: 0004-9425

PB CSIRO

DT Journal

LA English

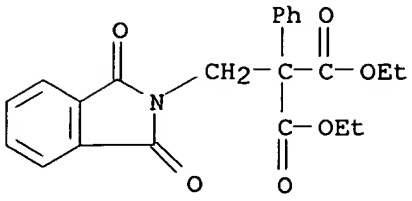
AB In an attempt to obtain new compds. with binding activity at the GABAB receptor site, 3-amino-2-arylpropanoic acids and their sulfonic, phosphonic, and hydroxamic acid analogs were prepared In addition, the isomer of phaclofen, 3-amino-1-(4-chlorophenyl)-propylphosphonic acid, and the higher homolog of baclofen, 5-amino-2-(4-chlorophenyl)pentanoic acid were prepared

IT **112864-34-3P 199436-87-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and GABA receptor antagonist activity of baclofen, phaclofen, and saclofen analogs)

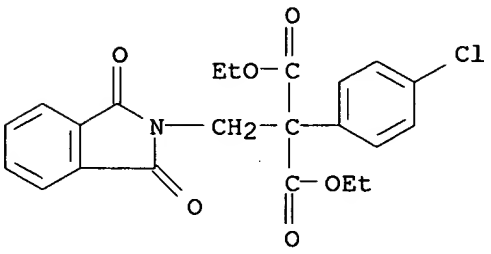
RN 112864-34-3 CAPLUS

CN Propanedioic acid, [(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenyl-

, diethyl ester (9CI) (CA INDEX NAME)



RN 199436-87-8 CAPLUS
CN Propanedioic acid, (4-chlorophenyl)[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)

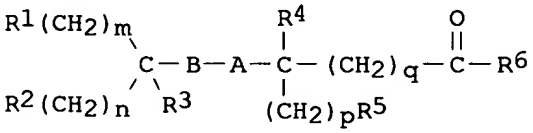


RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:204398 CAPLUS
DN 126:264353
TI Preparation of acylated amino acids as endothelin antagonists
IN Doherty, Annette M.; Hamilton, Harriet W.; Kaltenbronn, James S.; Quin, Iii John
PA Warner-Lambert Company, USA
SO U.S., 16 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5610177	A	19970311	US 1994-287389	19940808 <--
PRAI US 1994-287389		19940808		

OS MARPAT 126:264353
GI



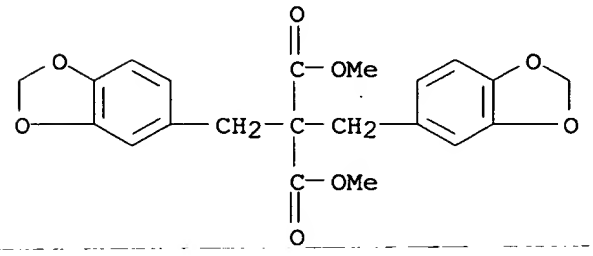
I

AB Novel acylated amino acids I [R1, R2 = independently partially or completely unsatd., (un)substituted aryl or heteroaryl, (un)substituted C3-5 cycloalkyl; m, n = independently 1-3; R3 = H, straight or branched C1-4 alkyl; B = CH:CH, (CH2)r, r = 0-3; A = CONH, NHCO, CH2NH, CSNH, COCH2, CONMe, NMeCO; R4 = straight or branched C1-4 alkyl or C2-4 alkenyl, benzyl substituted with 0-3 halo, alkoxy, or alkyl groups; p = 0-3; R5 = partially or completely unsatd., (un)substituted aryl or heteroaryl; q = 0-3; R6 = OR7, NR8R9; R7 = H, lower alkyl; R8, R9 = independently H, lower alkyl; NR8R9 = 3-7 membered heterocyclic ring containing not more than 2 hetero atoms, and where the heteroatoms are separated by 2 carbon atoms] which are antagonists of endothelin are described. Methods for their preparation and pharmaceutical compns. containing them are also included. Compds. I are expected to be useful in treating elevated levels of endothelin, acute and chronic renal failure, hypertension, myocardial infarction, myocardial ischemia, cerebral vasospasm, cirrhosis, septic shock, congestive heart failure, endotoxic shock, subarachnoid hemorrhage, arrhythmias, asthma, preeclampsia, atherosclerotic disorders including Raynaud's disease and restenosis, angina, cancer, pulmonary hypertension, ischemic disease, gastric mucosal damage, hemorrhagic shock, ischemic bowel disease, diabetes, head injury, and stroke. Thus, acylation of α-methyl-D-tryptophan Me ester with bis(1-naphthylmethyl)acetyl chloride, followed by saponification with LiOH, gave acyltryptophan derivative (1-C10H7CH2)2CHCO-α-Me-D-Trp-OH (II). II and 15 related N-acyl-α-methylamino acid derivs. showed in vitro inhibition of endothelin-3 (ET-3)-stimulated arachidonic acid release in cultured Chinese hamster ovary cells.

IT **188822-02-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of acylated amino acids as endothelin antagonists)

RN 188822-02-8 CAPLUS

CN Propanedioic acid, bis(1,3-benzodioxol-5-ylmethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 5 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:70350 CAPLUS

DN 126:199453

TI Preparation of adamantyl indolylalkylcarbamates and analogs as cholecystokinin antagonists

IN Horwell, David C.; Roberts, Edward; Holmes, Ann; Padia, Janak K.; Roark, William H.; Roth, Bruce D.; Trivedi, Bharat K.; Kleinschroth, Jurgen; Rees, David C.; Richardson, Reginald S.

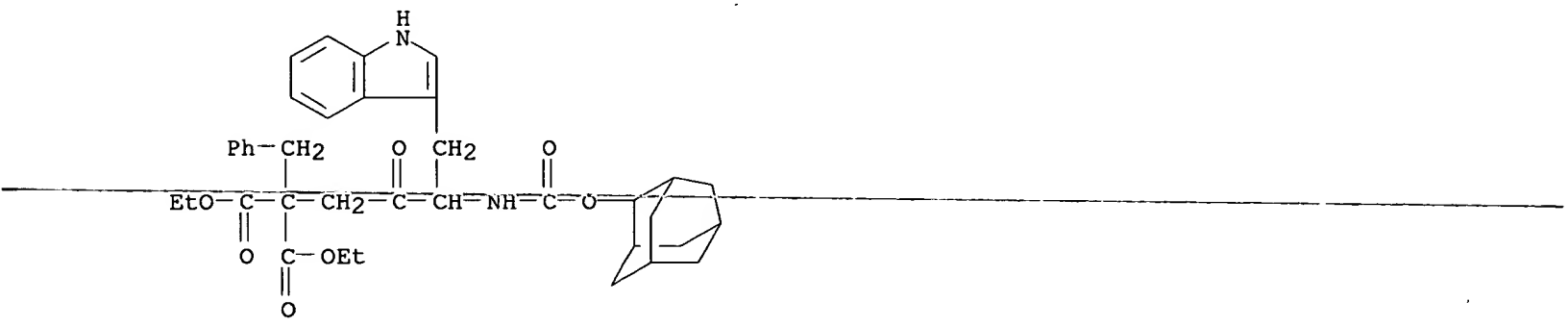
PA Warner-Lambert Company, USA

SO U.S., 77 pp., Cont.-in-part of U.S. Ser. No. 839, 647, abandoned.

CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5593967	A	19970114	US 1993-41647	19930401 <--
	ZA 9106922	A	19930301	ZA 1991-6922	19910830 <--
	US 5846942	A	19981208	US 1996-709316	19960909
PRAI	US 1990-576628	B2	19900831		
	US 1991-726655	B2	19910712		
	US 1992-839647	B2	19920221		
	US 1993-41647	A3	19930401		

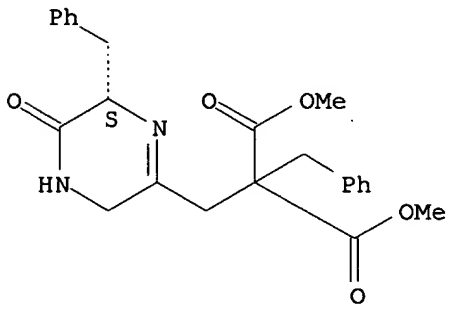
OS MARPAT 126:199453
AB R1AE(CH2)mCR2(CR5R6R7)n(CH2)pXq(CHR3)r(CHR4)sYt(CR20R12)u(CHR13)vR8 [I; A = bond, O, (alkyl)imino, etc.; E = bond, divalent amino acid residue, (CHR3)r, NHCO, CO2, etc.; R1 = (poly)cycloalkyl, heterocyclyl, etc.; R2,R20 = H, alkyl, vinyl, alkoxy(alkyl), aryl(alkyl), etc.; R3,R4 = groups cited for R2 or (CH2)nBD; B = bond, CO2(CH2)n, CONH(CH2)n, etc.; D = H, OH, CO2H, alkoxycarbonyl, CH2OH, alkoxymethyl, etc.; R5,R6 = H or alkyl; R7,R8 = cycloalkyl, (hetero)aryl, etc.; R12,R13 = H or (CH2)nBD; R12R13 = bond; X,Y = CONH, NHCO, CO2, CH2O, etc.; m,n,p-v = 0-6] were prepared Thus, R1O2CNHCHRCH2R7 (R1 = 2-adamantyl, R7 = 3-indolyl)(II; R = CO2H) was converted in 2 steps to (R)-II (III; R = CHO) which was reductively aminated by (S)-PhCH2CH(NH2)CH2OH to give III [R = (S)-CH2NHCH(CH2OH)CH2Ph]. Data for biol. activity of I were given.
IT **187610-06-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of adamantyl indolylalkylcarbamates and analogs as cholecystokinin antagonists)
RN 187610-06-6 CAPLUS
CN Propanedioic acid, [4-(1H-indol-3-yl)-2-oxo-3-[[(tricyclo[3.3.1.13,7]dec-2-yloxy)carbonyl]amino]butyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 6 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:807715 CAPLUS
DN 124:29697
TI 3,6-Dioxoperhydropyrrolo[1,2-a]pyrazines as templates for peptidomimetics
AU Martin-Martinez, Mercedes; Garcia-Lopez, M. Teresa; Herranz, Rosario; Gonzalez-Muniz, Rosario

CS Inst. Quim. Med. (CSIC), Madrid, 28006, Spain
SO Tetrahedron (**1995**), 51(37), 10361-74
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier
DT Journal
LA English
OS CASREACT 124:29697
AB The synthesis of 4,7-di- and 4,7,7-trisubstituted 3,6-dioxoperhydropyrrolo[1,2-a]pyrazine-7-carboxylate derivs. was described. The approach used for the preparation of this heterocyclic template was based on the reductive amination of 4-keto diesters derived from dipeptides. E.g., hydrogenation of Me 5-[(N-benzyloxycarbonyl)-L-alanyl]amino-2-methoxycarbonyl-4-oxopentanoate in MeOH in the presence of Pd/C gave 79% (4S,7R,8aR)-7-methoxycarbonyl-4-methyl-3,6-dioxoperhydropyrrolo[1,2-a]pyrazine and 15 % (4S,7S,8aS)-7-methoxycarbonyl-4-methyl-3,6-dioxoperhydropyrrolo[1,2-a]pyrazine.
IT **171513-60-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dioxoperhydropyrrolopyrazines as templates for peptidomimetics)
RN 171513-60-3 CAPLUS
CN Propanedioic acid, (phenylmethyl)[[3,4,5,6-tetrahydro-5-oxo-6-(phenylmethyl)pyrazinyl]methyl]-, dimethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



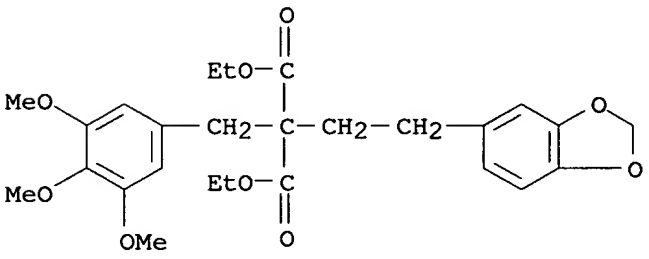
L5 ANSWER 7 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:410368 CAPLUS
DN 122:187373
TI Preparation of polycyclic compounds as phosphodiesterases inhibitors
IN Tanaka, Masahide; Wakamatsu, Takeshi; Mitsuhashi, Hiroshi; Sato, Toshitsugu
PA Tsumura and Co., Japan
SO Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 594890	A1	19940504	EP 1992-118620	19921030 <--
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL				

PRAI EP 1992-118620 19921030
OS MARPAT 122:187373
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I (R1-R8 = H, HO, (substituted) alkoxy or PhCH2O, neighboring 2 of R1-R8 = (substituted) alkylene; A = Q wherein X = HC, N), are prepared To (RS)-(E)-3-[1-(3,4-dihydroxy-5-methoxyphenyl)methyl]-(3,4,5-trimethoxybenzylidene)butanol in CH2Cl2 and F3CCO2H was added Fe(ClO4)3 to give (3aRS,SRbiar)-II which at 500 μM inhibited bovine heart phosphodiesterase 90.5%.
IT **58745-52-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polycyclic compds. as phosphodiesterases inhibitors)
RN 58745-52-1 CAPLUS
CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(3,4,5-trimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 8 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:294083 CAPLUS
DN 123:285785
TI Preparation of aromatic amidine derivatives as inhibitors of human blood coagulation factor for treatment and prevention of influenza
IN Ikeuchi, Kyoshi; Takase, Hiroyuki; Murakami, Yoichi
PA Daiichi Seiyaku Co, Japan
SO Jpn. Kokai Tokkyo Koho, 79 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06227971	A2	19940816	JP 1993-17536	19930204 <--
	JP 3457694	B2	20031020		

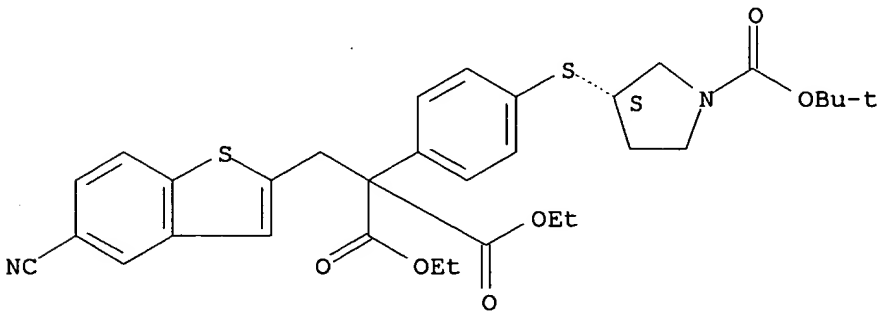
PRAI JP 1993-17536 19930204
OS MARPAT 123:285785
GI For diagram(s), see printed CA Issue.
AB The title compds. [I; R1 = H, alkoxy; R2 = H, alkyl, alkoxy, CO2H, alkoxycarbonyl, carboxyalkyl, alkoxycarbonylalkyl; R3 = H, CO2H, alkoxycarbonyl, carboxyalkyl, alkoxycarbonylalkyl, carboxyalkoxy, alkoxycarbonylalkoxy; R4 = H, OH, alkyl, alkoxy; A = C1-4 alkylene which

may be substituted by 1-2 of hydroxyalkyl, CO2H, alkoxycarbonyl, carboxyalkyl, and alkoxycarbonylalkyl; X = single bond, O, S, CO; Y = 5- or 6-membered (un)saturated carbocyclyl or heterocyclyl, NH2, or aminoalkyl each of which may be substituted; ring Z = pyrrole, 1,2-dihydropyrrole, furan, thiofuran, imidazole, oxazole, thiazole, benzene, tetrahydrobenzene, or cyclopentadiene ring] are prepared Thus, Et 3-(5-cyano-2-benzofuranyl)-2-(4-hydroxyphenyl)propionate was condensed with (2S)-1-tert-butoxycarbonyl-2-pyrrolidinemethanol in the presence of Ph3P and di-Et azodicarboxylate in THF to give ether (II; R = cyano, R5 = Me3CO2C) which was treated with HCl(g) in ethanol and then with NH3 in EtOH to give amidine II.2HCl (R = amidino, R5 = H). Title compound (III.2HCl) showed IC50 of 5.04 μg/mL against human blood coagulation.

IT **150610-90-5P 150611-01-1P 150611-03-3P 150613-30-2P 150613-81-3P 167979-40-0P 167979-41-1P 167979-51-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate for preparation of aromatic amidine derivs. as inhibitors of human blood coagulation factor)

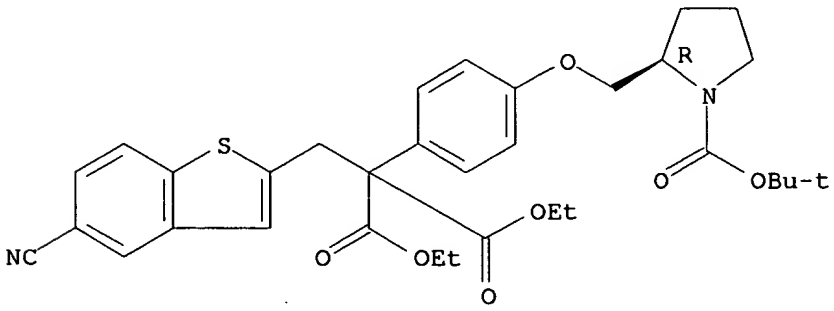
RN 150610-90-5 CAPLUS
CN Propanedioic acid, [(5-cyanobenzo[b]thien-2-yl)methyl][4-[[1-[(1,1-dimethylethoxy)carbonyl]-3-pyrrolidinyl]thio]phenyl]-, diethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



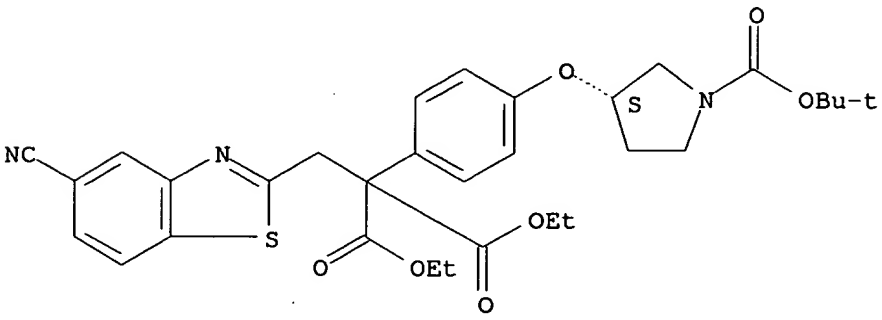
RN 150611-01-1 CAPLUS
CN Propanedioic acid, [(5-cyanobenzo[b]thien-2-yl)methyl][4-[[1-[(1,1-dimethylethoxy)carbonyl]-2-pyrrolidinyl]methoxy]phenyl]-, diethyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

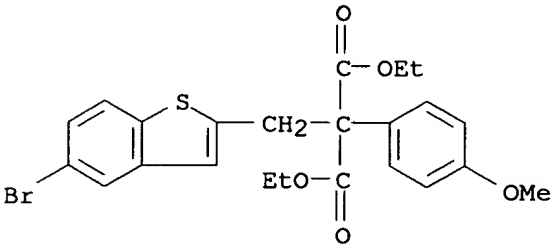


RN 150611-03-3 CAPLUS
CN Propanedioic acid, [(5-cyano-2-benzothiazolyl)methyl][4-[[(3S)-1-[(1,1-dimethylethoxy)carbonyl]-3-pyrrolidinyl]oxy]phenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

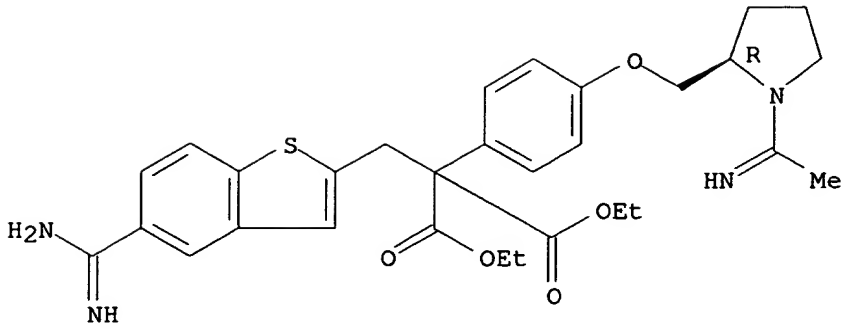


RN 150613-30-2 CAPLUS
CN Propanedioic acid, [(5-bromobenzo[b]thien-2-yl)methyl](4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



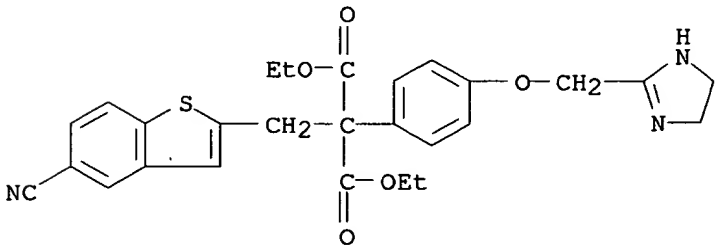
RN 150613-81-3 CAPLUS
CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl]methyl][4-[[1-(1-iminoethyl)-2-pyrrolidinyl]methoxy]phenyl]-, diethyl ester, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



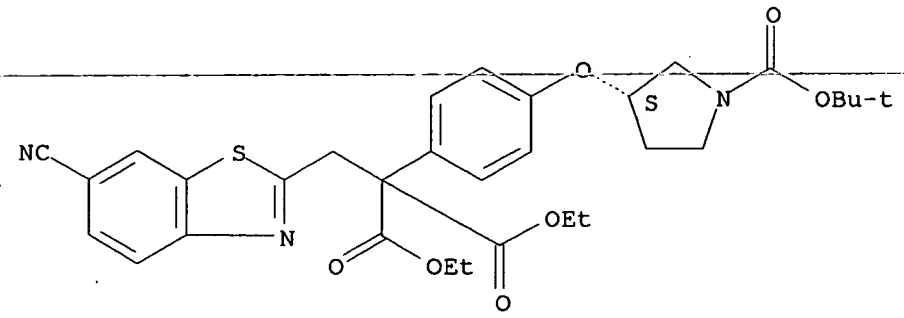
●2 HCl

RN 167979-40-0 CAPLUS
CN Propanedioic acid, [(5-cyanobenzo[b]thien-2-yl)methyl][4-[(4,5-dihydro-1H-imidazol-2-yl)methoxy]phenyl]-, diethyl ester (9CI) (CA INDEX NAME)



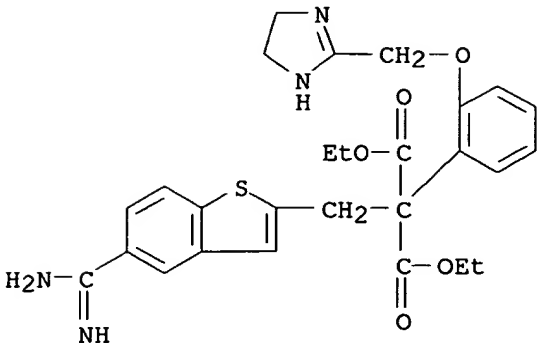
RN 167979-41-1 CAPLUS
CN Propanedioic acid, [(6-cyano-2-benzothiazolyl)methyl][4-[[(3S)-1-[(1,1-dimethylethoxy)carbonyl]-3-pyrrolidinyl]oxy]phenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 167979-51-3 CAPLUS
CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl]methyl][2-[(4,5-dihydro-1H-imidazol-2-yl)methoxy]phenyl]-, diethyl ester,

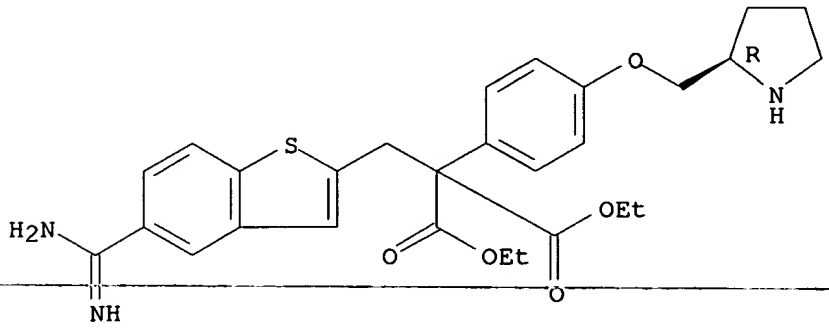
dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

IT **150613-80-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aromatic amidine derivs. as inhibitors of human blood coagulation factor for treatment and prevention of influenza)
RN 150613-80-2 CAPLUS
CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl]methyl][4-(2-pyrrolidinylmethoxy)phenyl]-, diethyl ester, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L5 ANSWER 9 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:107001 CAPLUS
DN 120:107001
TI Heterocyclic and aromatic amidine derivatives and salts thereof
IN Nagahara, Takayasu; Kanaya, Naoaki; Inamura, Kazue; Yokoyama, Yukio

PA Daiichi Pharmaceutical Co., Ltd., Japan
SO Eur. Pat. Appl., 94 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 540051	A1	19930505	EP 1992-118705	19921030	<--
	EP 540051	B1	19960403			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
	ZA 9208276	A	19930506	ZA 1992-8276	19921026	<--
	IL 103564	A1	19981206	IL 1992-103564	19921027	
	NO 9204164	A	19930503	NO 1992-4164	19921029	<--
	DE 4236574	A1	19930506	DE 1992-4236574	19921029	<--
	CA 2081836	AA	19930501	CA 1992-2081836	19921030	<--
	AU 9227470	A1	19930506	AU 1992-27470	19921030	<--
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	JP 05208946	A2	19930820	JP 1992-292892	19921030	<--
	JP 2879718	B2	19990405			
	US 5300851	A	19940405	US 1992-969369	19921030	<--
	HU 65890	A2	19940728	HU 1992-3433	19921030	<--
	AT 136293	E	19960415	AT 1992-118705	19921030	<--
	ES 2088073	T3	19960801	ES 1992-118705	19921030	<--
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	JP 10291931	A2	19981104	JP 1998-85454	19921030	<--
	JP 3461441	B2	20031027			
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	SK 279807	B6	19990413	SK 1992-3276	19921030	
	RU 2139851	C1	19991020	RU 1992-4542	19921030	
	SG 78251	A1	20010220	SG 1996-6031	19921030	
	FI 107923	B1	20011031	FI 1992-4932	19921030	
	CN 1072677	A	19930602	CN 1992-114304	19921031	<--
	CN 1049434	B	20000216			
	KR 205152	B1	19990701	KR 1992-20309	19921031	
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	CN 1168885	A	19971231	CN 1997-110745	19970416	<--
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	CN 1062865	B	20010307			
	US 5866577	A	19990202	US 1997-924504	19970905	
	US 5962695	A	19991005	US 1998-131235	19980807	
PRAI	JP 1991-286088	A	19911031			
	JP 1991-285919	A	19911031			
	JP 1992-292892	A3	19921030			
	US 1992-969369	B1	19921030			
	US 1992-969396	B1	19921030			
	US 1994-282571	B3	19940729			
	US 1995-469593	A1	19950606			
	US 1997-924504	A3	19970905			

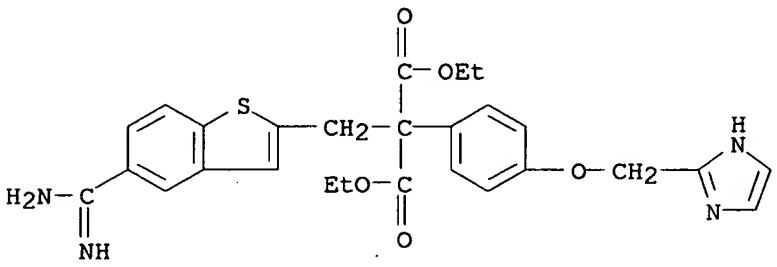
OS MARPAT 120:107001
GI For diagram(s), see printed CA Issue.
AB The title compds. I (where the benzeno-Z ring is indolyl, benzimidazolyl, naphthyl, etc.; R = HN:CNH2; R1 = H, alkoxy; R2 = H, alkyl, alkoxy, etc.; R3 = H, carboxyl, etc.; R4 = H, OH, alkyl, alkoxy; A = C1-4 alkylene; X = single bond, O, S, CO; n = 0-4; Y = heterocyclic or cyclic hydrocarbon

moiety) useful as anticoagulant agents were prepared by treating I (R = CN) with R5OH (R5 = alkyl) to give I (R = R5OC:NH) followed by treatment with NH3. Some of the prepared compds. showed strong anticoagulant activity through their specific anti-FXa activity in comparison with DABE.

IT **150613-79-9P 150613-81-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

RN 150613-79-9 CAPLUS

CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl]methyl][4-(1H-imidazol-2-ylmethoxy)phenyl]-, diethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

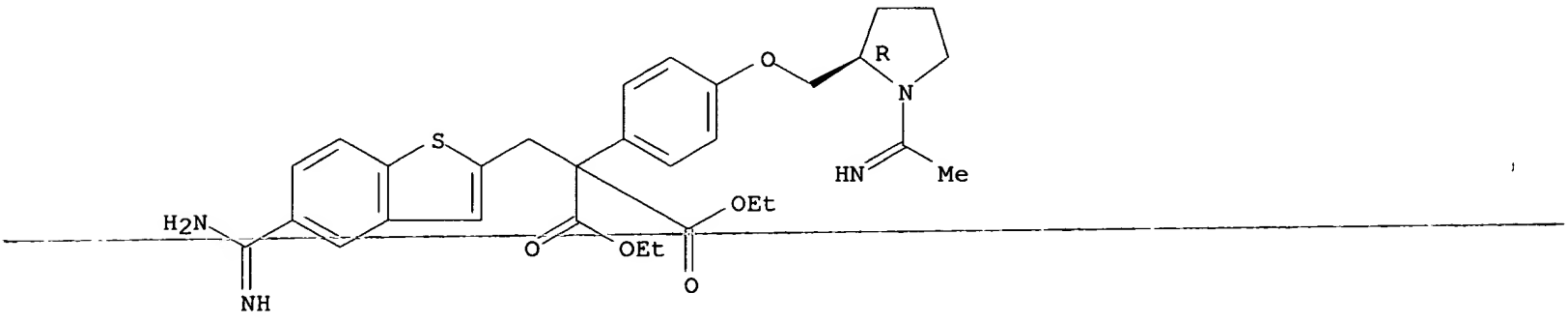


●2 HCl

RN 150613-81-3 CAPLUS

CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl]methyl][4-[[1-(1-iminoethyl)-2-pyrrolidinyl]methoxy]phenyl]-, diethyl ester, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

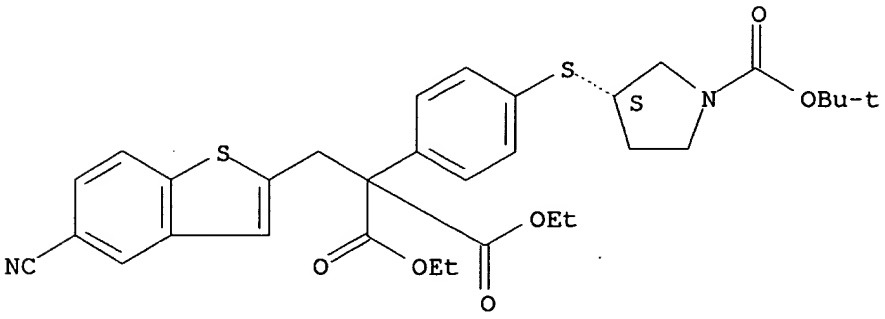
IT **150610-90-5P 150611-01-1P 150611-02-2P**
150611-03-3P 150613-30-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in preparation of amidine anticoagulants)

RN 150610-90-5 CAPLUS

CN Propanedioic acid, [(5-cyanobenzo[b]thien-2-yl)methyl][4-[[1-[(1,1-dimethylethoxy)carbonyl]-3-pyrrolidinyl]thio]phenyl]-, diethyl ester, (S)-(9CI) (CA INDEX NAME)

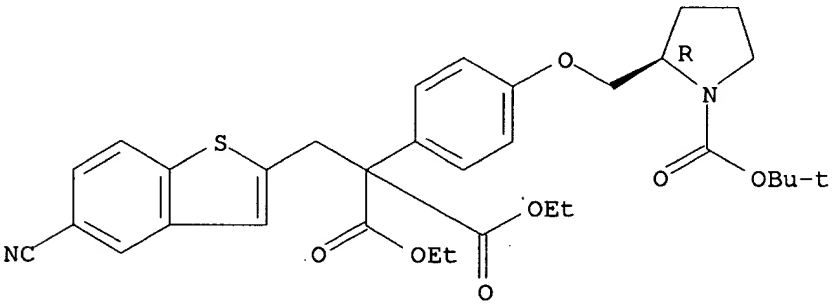
Absolute stereochemistry.



RN 150611-01-1 CAPLUS

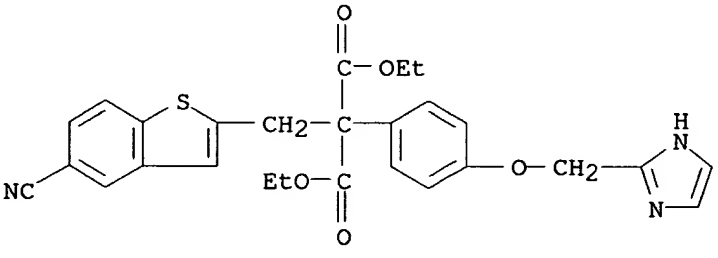
CN Propanedioic acid, [(5-cyanobenzo[b]thien-2-yl)methyl][4-[[1-[(1,1-dimethylethoxy)carbonyl]-2-pyrrolidinyl]methoxy]phenyl]-, diethyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 150611-02-2 CAPLUS

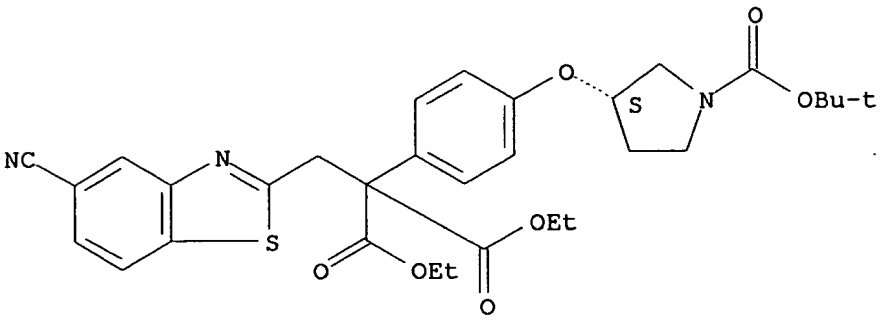
CN Propanedioic acid, [(5-cyanobenzo[b]thien-2-yl)methyl][4-(1H-imidazol-2-ylmethoxy)phenyl]-, diethyl ester (9CI) (CA INDEX NAME)



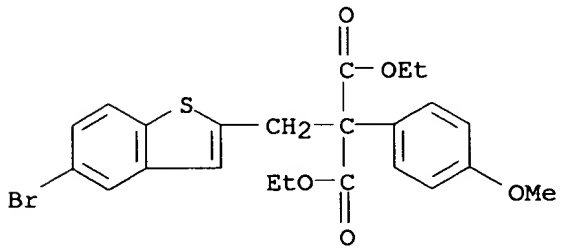
RN 150611-03-3 CAPLUS

CN Propanedioic acid, [(5-cyano-2-benzothiazolyl)methyl][4-[[(3S)-1-[(1,1-dimethylethoxy)carbonyl]-3-pyrrolidinyl]oxy]phenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

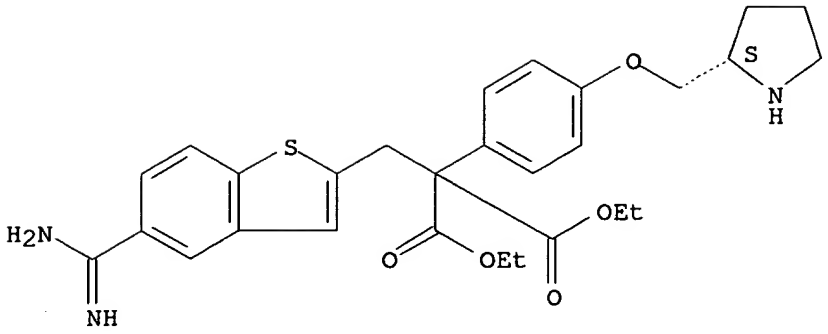


RN 150613-30-2 CAPLUS
CN Propanedioic acid, [(5-bromobenzo[b]thien-2-yl)methyl](4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



IT **150612-15-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as anticoagulants)
RN 150612-15-0 CAPLUS
CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl]methyl][4-(2-pyrrolidinylmethoxy)phenyl]-, diethyl ester, dihydrochloride, (S)- (9CI) (CA INDEX NAME)

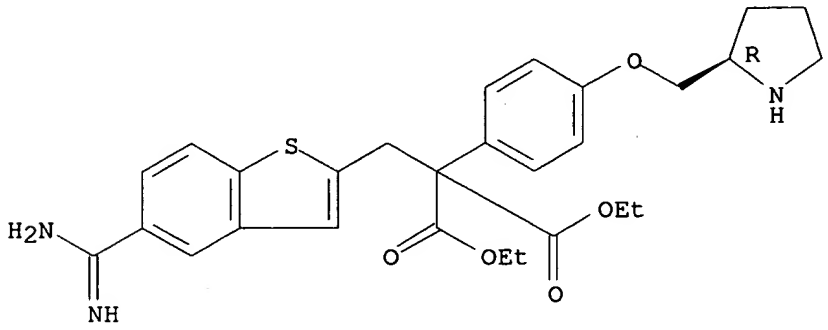
Absolute stereochemistry.



●2 HCl

IT **150613-80-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with Et acetimidate)
RN 150613-80-2 CAPLUS
CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl]methyl][4-(2-pyrrolidinylmethoxy)phenyl]-, diethyl ester, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L5 ANSWER 10 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:603418 CAPLUS
DN 119:203418
TI Preparation of azole derivative herbicides and fungicides
IN West, Peter John; Cornell, Clive Leonard; Briggs, Geoffrey Gower; Buehmann, Ulrich
PA Schering Agrochemicals Ltd., UK
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9311118	A1	19930610	WO 1992-EP2723	19921125 <--
	W: AU, BG, BR, CA, CS, FI, HU, JP, KR, NO, PL, RO, RU, SD, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
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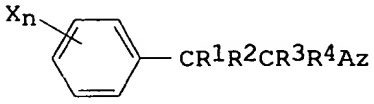
	EP 619812	A1	19941019	EP 1992-923799	19921125 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 07501801	T2	19950223	JP 1992-509801	19921125 <--
	HU 68182	A2	19950313	HU 1994-1466	19921125 <--
	BR 9206862	A	19951121	BR 1992-6862	19921125 <--
	ZA 9209336	A	19930802	ZA 1992-9336	19921202 <--
	CN 1075478	A	19930825	CN 1992-115306	19921204 <--
	FI 9402596	A	19940602	FI 1994-2596	19940602 <--
PRAI	GB 1991-25791	A	19911204		
	WO 1992-EP2723	A	19921125		

OS MARPAT 119:203418
GI



I

AB Title compds. I (Az = imidazol-1-yl, 1,2,4-triazol-1-yl; X = halo, HO2C, O2N, NC, R5O2C wherein R5 = (substituted) alkenyl, etc.; R1 = R5CO, R5O2C, HS, R5(O)pS wherein p = 0-2; R2 = NC, R5CO, O2N, aryl, aralkyl, heteroaryl, etc.; R3, R4 = H, (substituted) alkyl, aryl, heteroaryl; n = 0-4), are prepared 2,4-Cl2C6H3CH2CO2Pr (preparation given) was added to lithium diisopropylamide in THF followed by ClCO2Pr to give di-Pr (2,4-dichlorophenyl)malonate which in MeOCH2CH2OMe was treated with NaI and 1-(chloromethyl)-1H-1,2,4-triazole to give I (Az = 1,2,4-triazol-1-yl, Xn = 2,4-Cl2C6H3, R1 = R2 = PrO2C, R3 = R4 = H). A similar prepared compound I (Az = 1,2,4-triazol-1-yl, Xn = 2-(OMe)C6H4, R1 = R2 = PrO2C, R3 = R4 = H) at 2.0 kg/ha was effective 90-100% against blackgrass, couch, scentless mayweed and Buxbaum's speedwell.

IT **150441-89-7P 150441-91-1P 150441-92-2P**
150441-93-3P 150441-94-4P 150441-95-5P
150441-96-6P 150441-97-7P 150441-98-8P
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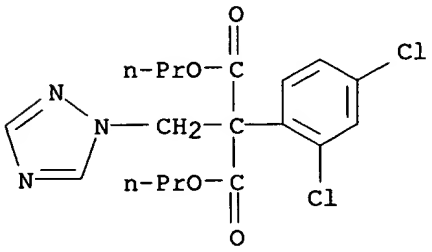
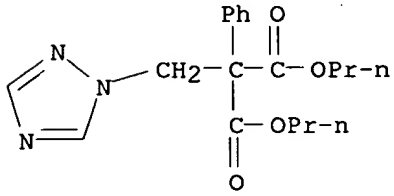
150442-89-0P 150442-91-4P 150443-02-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as agrochem. fungicide and herbicide)

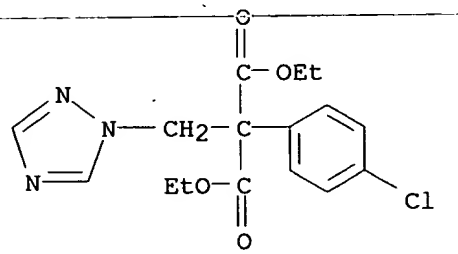
RN 150441-89-7 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



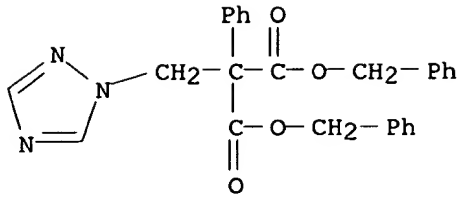
RN 150441-91-1 CAPLUS
CN Propanedioic acid, phenyl(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



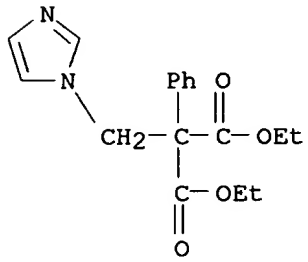
RN 150441-92-2 CAPLUS
CN Propanedioic acid, (4-chlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



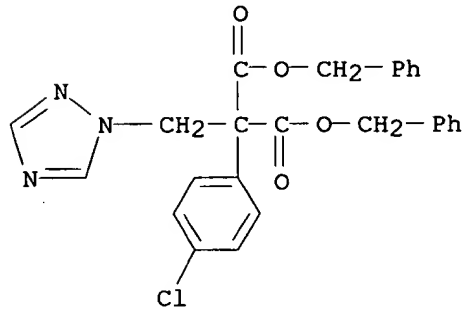
RN 150441-93-3 CAPLUS
CN Propanedioic acid, phenyl(1H-1,2,4-triazol-1-ylmethyl)-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



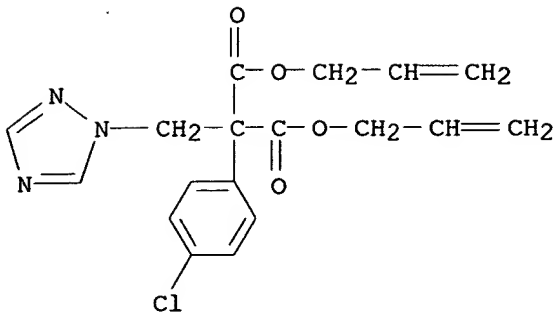
RN 150441-94-4 CAPLUS
CN Propanedioic acid, (1H-imidazol-1-ylmethyl)phenyl-, diethyl ester (9CI) (CA INDEX NAME)



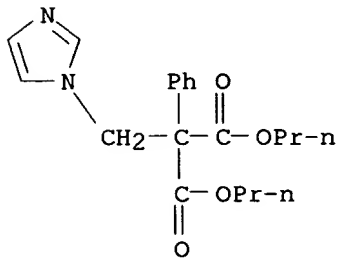
RN 150441-95-5 CAPLUS
CN Propanedioic acid, (4-chlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



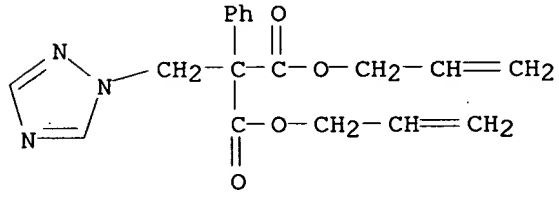
RN 150441-96-6 CAPLUS
CN Propanedioic acid, (4-chlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, di-2-propenyl ester (9CI) (CA INDEX NAME)



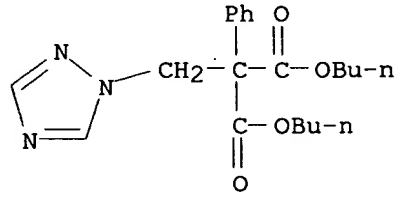
RN 150441-97-7 CAPLUS
CN Propanedioic acid, (1H-imidazol-1-ylmethyl)phenyl-, dipropyl ester (9CI) (CA INDEX NAME)



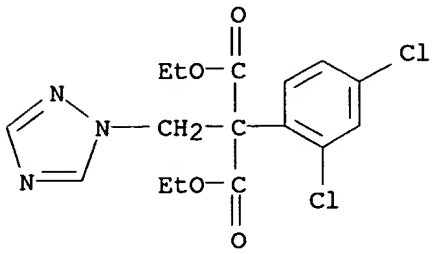
RN 150441-98-8 CAPLUS
CN Propanedioic acid, phenyl(1H-1,2,4-triazol-1-ylmethyl)-, di-2-propenyl ester (9CI) (CA INDEX NAME)



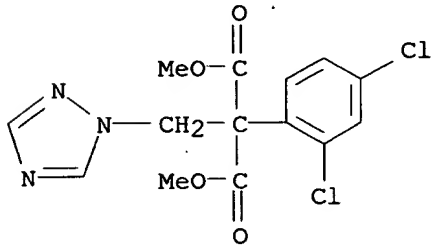
RN 150441-99-9 CAPLUS
CN Propanedioic acid, phenyl(1H-1,2,4-triazol-1-ylmethyl)-, dibutyl ester (9CI) (CA INDEX NAME)



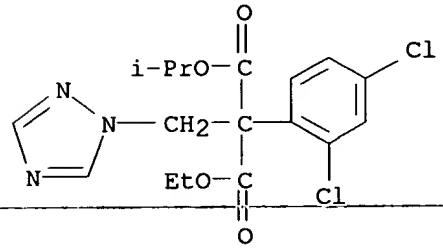
RN 150442-00-5 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



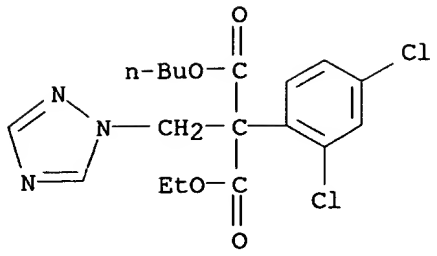
RN 150442-01-6 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



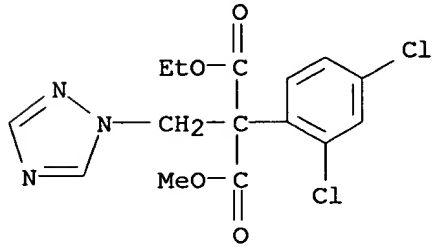
RN 150442-02-7 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, ethyl 1-methylethyl ester (9CI) (CA INDEX NAME)



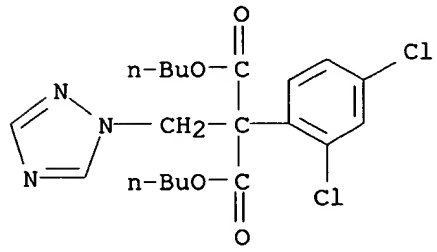
RN 150442-03-8 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, butyl ethyl ester (9CI) (CA INDEX NAME)



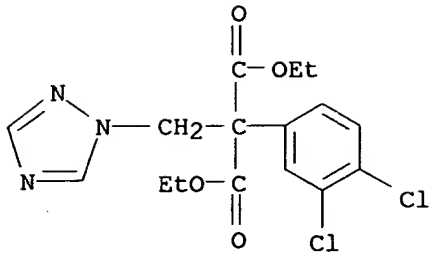
RN 150442-04-9 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, ethyl methyl ester (9CI) (CA INDEX NAME)



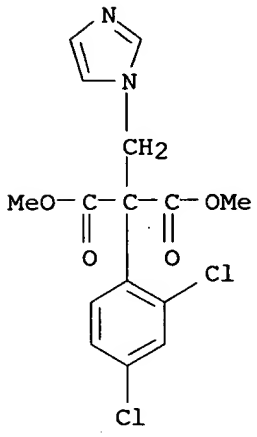
RN 150442-07-2 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dibutyl ester (9CI) (CA INDEX NAME)



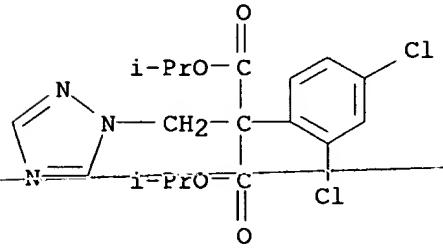
RN 150442-08-3 CAPLUS
CN Propanedioic acid, (3,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



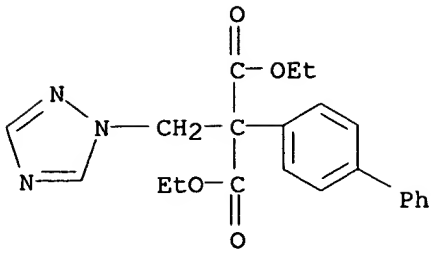
RN 150442-09-4 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-imidazol-1-ylmethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



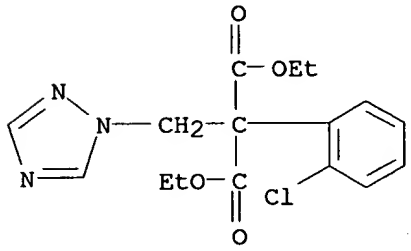
RN 150442-10-7 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, bis(1-methylethyl) ester (9CI) (CA INDEX NAME)



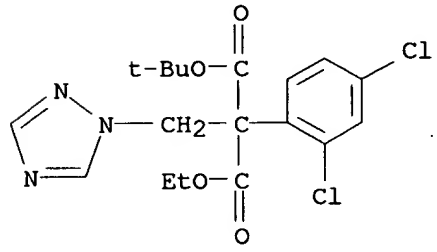
RN 150442-11-8 CAPLUS
CN Propanedioic acid, [1,1'-biphenyl]-4-yl(1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



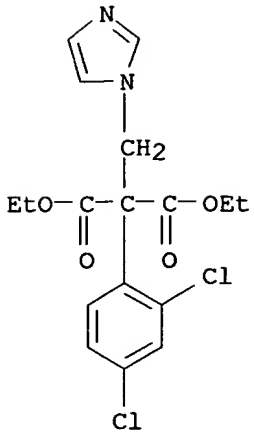
RN 150442-12-9 CAPLUS
CN Propanedioic acid, (2-chlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



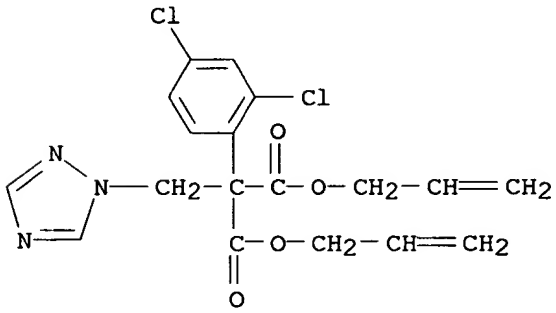
RN 150442-13-0 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, 1,1-dimethylethyl ethyl ester (9CI) (CA INDEX NAME)



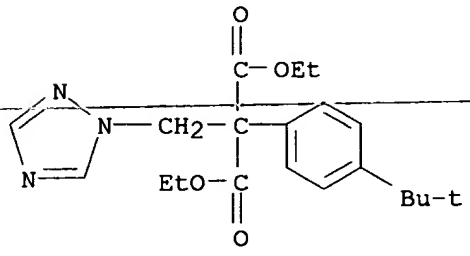
RN 150442-15-2 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-imidazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



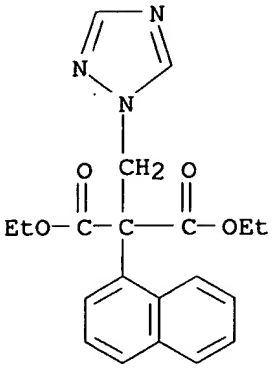
RN 150442-16-3 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, di-2-propenyl ester (9CI) (CA INDEX NAME)



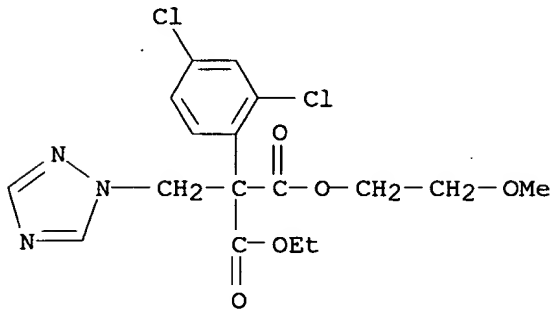
RN 150442-19-6 CAPLUS
CN Propanedioic acid, [4-(1,1-dimethylethyl)phenyl](1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



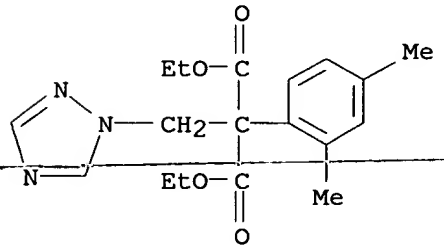
RN 150442-23-2 CAPLUS
CN Propanedioic acid, 1-naphthalenyl(1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



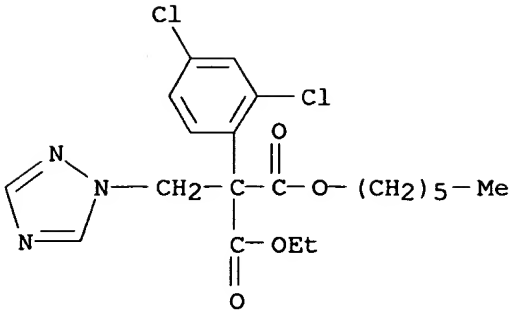
RN 150442-24-3 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, ethyl 2-methoxyethyl ester (9CI) (CA INDEX NAME)



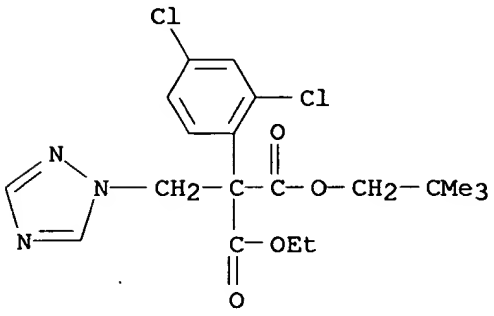
RN 150442-28-7 CAPLUS
CN Propanedioic acid, (2,4-dimethylphenyl)(1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



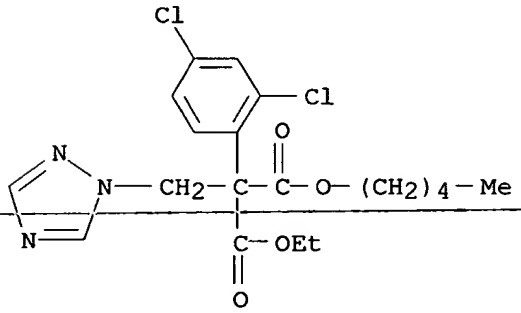
RN 150442-30-1 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, ethyl hexyl ester (9CI) (CA INDEX NAME)



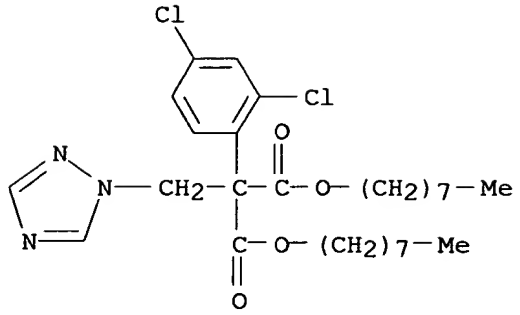
RN 150442-31-2 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, 2,2-dimethylpropyl ethyl ester (9CI) (CA INDEX NAME)



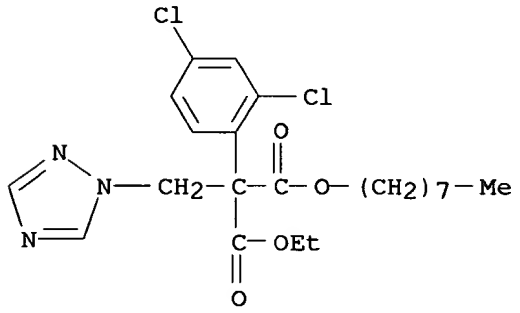
RN 150442-32-3 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, ethyl pentyl ester (9CI) (CA INDEX NAME)



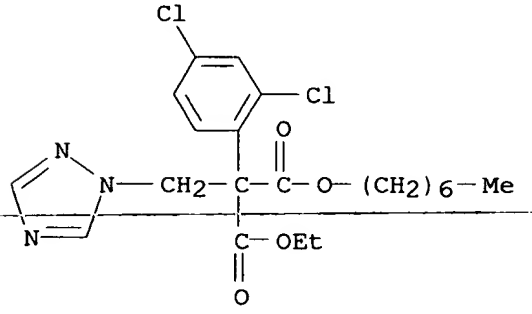
RN 150442-33-4 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dioctyl ester (9CI) (CA INDEX NAME)



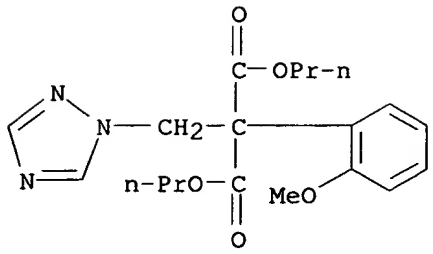
RN 150442-34-5 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, ethyl octyl ester (9CI) (CA INDEX NAME)



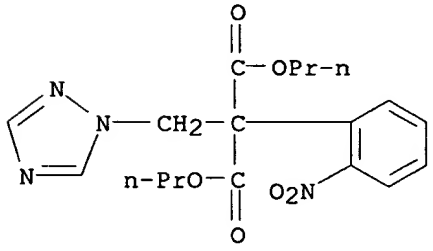
RN 150442-35-6 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, ethyl heptyl ester (9CI) (CA INDEX NAME)



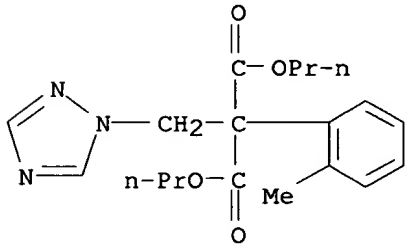
RN 150442-36-7 CAPLUS
CN Propanedioic acid, (2-methoxyphenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



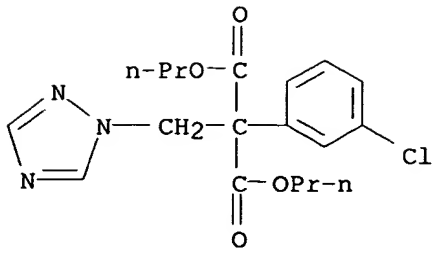
RN 150442-37-8 CAPLUS
CN Propanedioic acid, (2-nitrophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



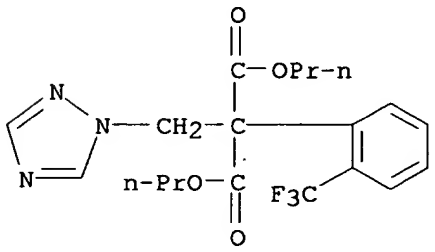
RN 150442-38-9 CAPLUS
CN Propanedioic acid, (2-methylphenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



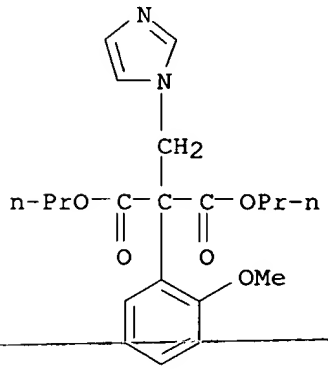
RN 150442-39-0 CAPLUS
CN Propanedioic acid, (3-chlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



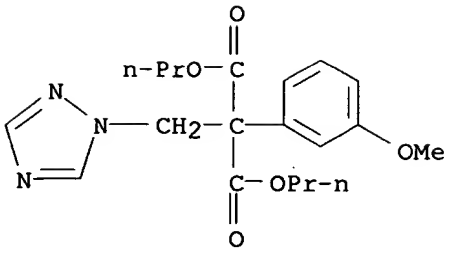
RN 150442-40-3 CAPLUS
CN Propanedioic acid, (1H-1,2,4-triazol-1-ylmethyl)[2-(trifluoromethyl)phenyl]-, dipropyl ester (9CI) (CA INDEX NAME)



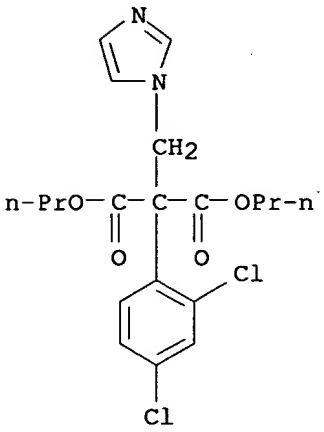
RN 150442-41-4 CAPLUS
CN Propanedioic acid, (1H-imidazol-1-ylmethyl)(2-methoxyphenyl)-, dipropyl ester (9CI) (CA INDEX NAME)



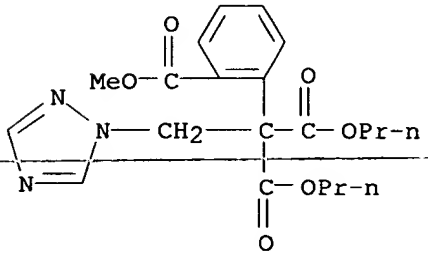
RN 150442-43-6 CAPLUS
CN Propanedioic acid, (3-methoxyphenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



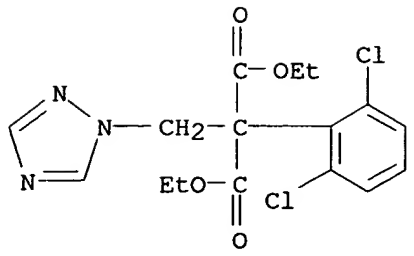
RN 150442-44-7 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)(1H-imidazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



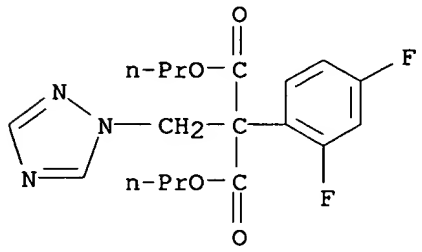
RN 150442-45-8 CAPLUS
CN Propanedioic acid, [2-(methoxycarbonyl)phenyl](1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



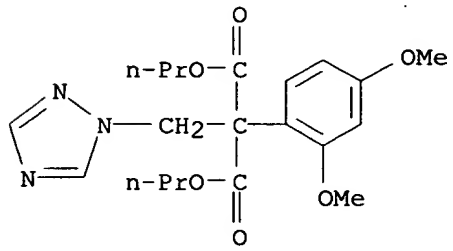
RN 150442-47-0 CAPLUS
CN Propanedioic acid, (2,6-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



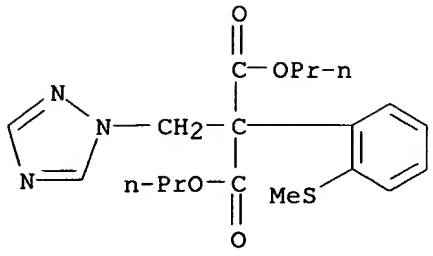
RN 150442-51-6 CAPLUS
CN Propanedioic acid, (2,4-difluorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



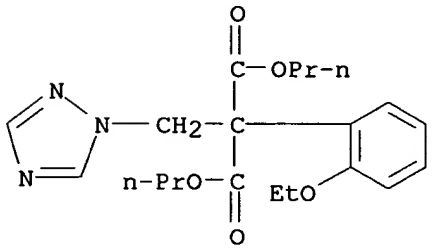
RN 150442-52-7 CAPLUS
CN Propanedioic acid, (2,4-dimethoxyphenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



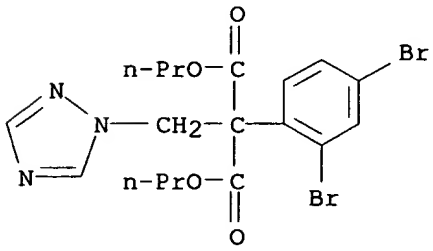
RN 150442-55-0 CAPLUS
CN Propanedioic acid, [2-(methylthio)phenyl](1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



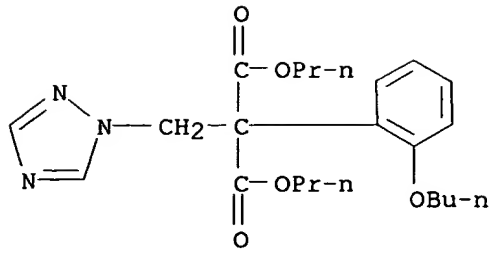
RN 150442-56-1 CAPLUS
CN Propanedioic acid, (2-ethoxyphenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



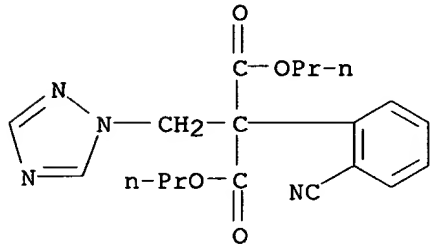
RN 150442-58-3 CAPLUS
CN Propanedioic acid, (2,4-dibromophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



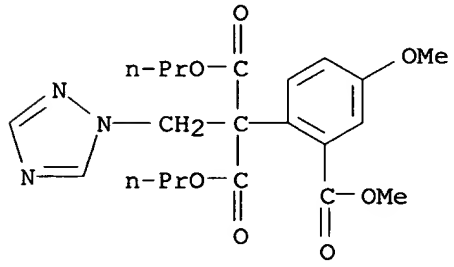
RN 150442-61-8 CAPLUS
CN Propanedioic acid, (2-butoxyphenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



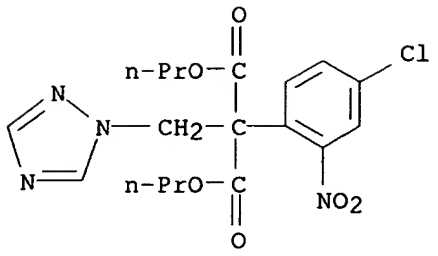
RN 150442-62-9 CAPLUS
CN Propanedioic acid, (2-cyanophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



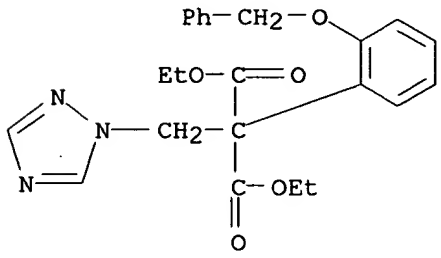
RN 150442-69-6 CAPLUS
CN Propanedioic acid, [4-methoxy-2-(methoxycarbonyl)phenyl](1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



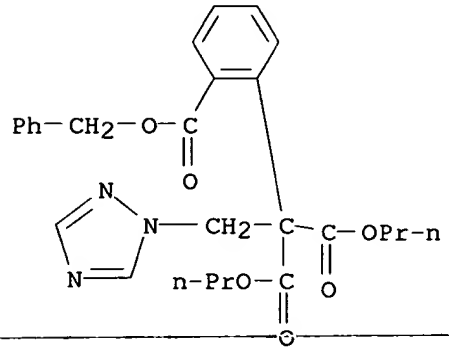
RN 150442-70-9 CAPLUS
CN Propanedioic acid, (4-chloro-2-nitrophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



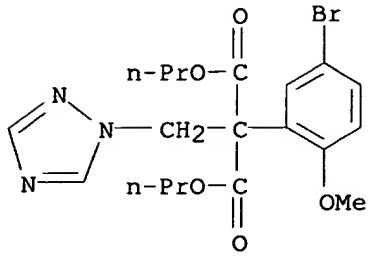
RN 150442-71-0 CAPLUS
CN Propanedioic acid, [2-(phenylmethoxy)phenyl](1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



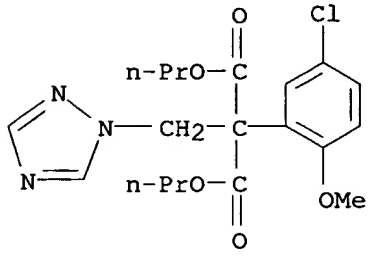
RN 150442-72-1 CAPLUS
CN Propanedioic acid, [2-[(phenylmethoxy)carbonyl]phenyl](1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



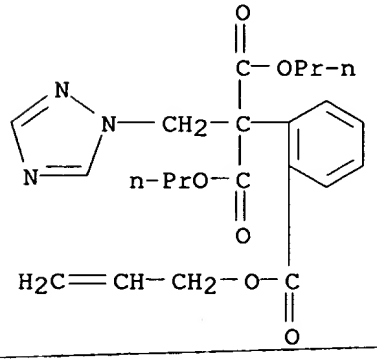
RN 150442-73-2 CAPLUS
CN Propanedioic acid, (5-bromo-2-methoxyphenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



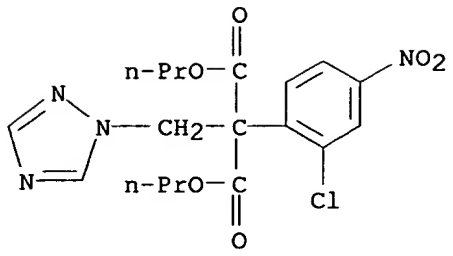
RN 150442-76-5 CAPLUS
CN Propanedioic acid, (5-chloro-2-methoxyphenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



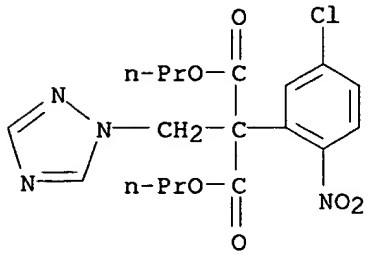
RN 150442-77-6 CAPLUS
CN Propanedioic acid, [2-[(2-propenyloxy)carbonyl]phenyl](1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



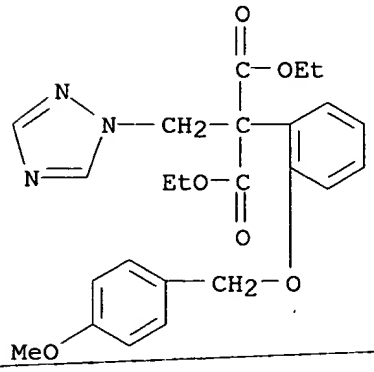
RN 150442-78-7 CAPLUS
CN Propanedioic acid, (2-chloro-4-nitrophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



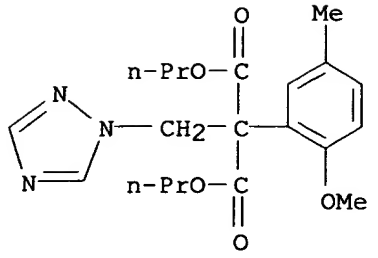
RN 150442-84-5 CAPLUS
CN Propanedioic acid, (5-chloro-2-nitrophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



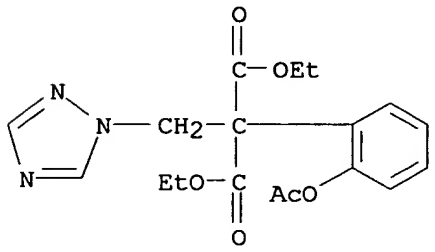
RN 150442-86-7 CAPLUS
CN Propanedioic acid, [2-[(4-methoxyphenyl)methoxy]phenyl](1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



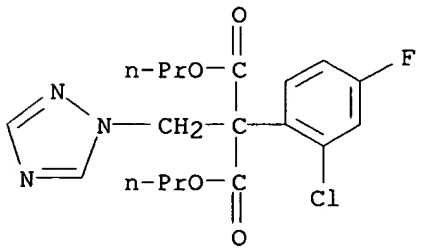
RN 150442-87-8 CAPLUS
CN Propanedioic acid, (2-methoxy-5-methylphenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



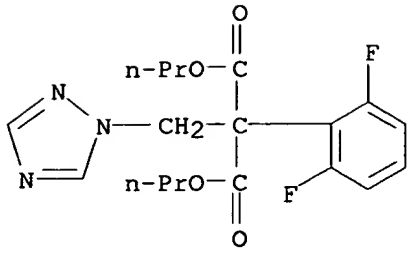
RN 150442-88-9 CAPLUS
CN Propanedioic acid, [2-(acetyloxy)phenyl](1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



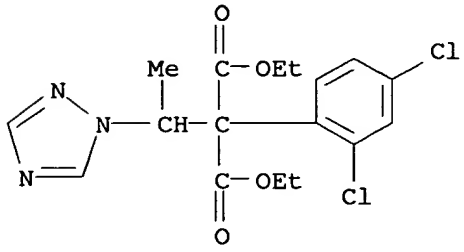
RN 150442-89-0 CAPLUS
CN Propanedioic acid, (2-chloro-4-fluorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



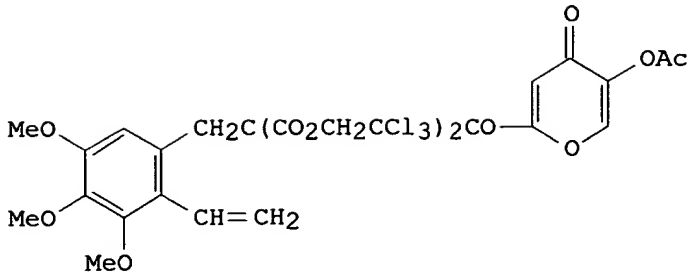
RN 150442-91-4 CAPLUS
CN Propanedioic acid, (2,6-difluorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



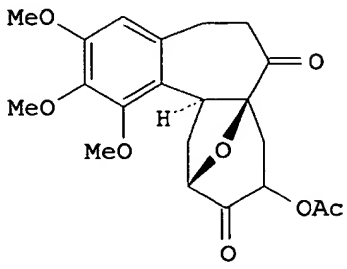
RN 150443-02-0 CAPLUS
CN Propanedioic acid, (2,4-dichlorophenyl)[1-(1H-1,2,4-triazol-1-yl)ethyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 11 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:517588 CAPLUS
DN 119:117588
TI Cycloadditions of 4-pyrones. An approach to colchicine
AU McBride, Bill J.; Garst, Michael E.
CS Dep. Chem., Univ. California, San Diego, La Jolla, CA, 92093, USA
SO Tetrahedron (**1993**), 49(14), 2839-54
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
OS CASREACT 119:117588
GI



I



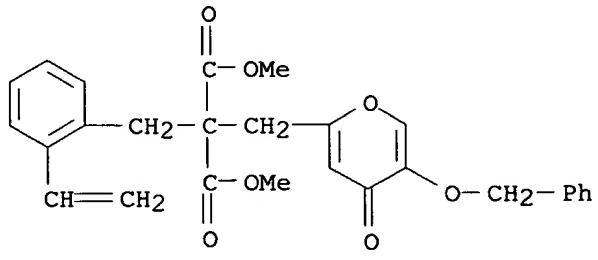
II

AB The 4-pyrone, [5-acetoxy-4-oxo-4H-pyran-2-yl]carbonyl chloride was coupled with the malonate anion of bis(2,2,2-trichloroethyl) 2-ethenyl-3,4,5-trimethoxybenzylpropanedioate and analogs thereof to give the pyranylcarbonyl(ethenylbenzyl)propanedioate adduct I and the corresponding analogs. These adducts then underwent intramol. thermal cyclizations (61-100% yield) to form the two fused seven member rings of the carbon skeleton of colchicine. The malonate moiety was deprotected and decarboxylated quant. to provide the desired epoxybenzoheptalenedione II which contained a bridging ether, from C7a to C11 in the C ring, and a ketone at the 7 position. Removal of the bridging ether as H2O would yield the desired tropolone. Attempts to remove the ether bridge were unsuccessful.

IT **149296-22-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of)

RN 149296-22-0 CAPLUS

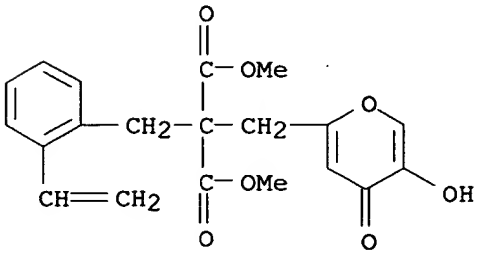
CN Propanedioic acid, [(2-ethenylphenyl)methyl][[4-oxo-5-(phenylmethoxy)-4H-pyran-2-yl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)



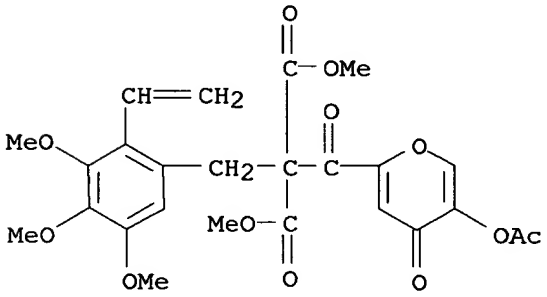
IT **87057-53-2P 149295-99-8P 149296-01-5P 149296-03-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and intramol. cyclization of)

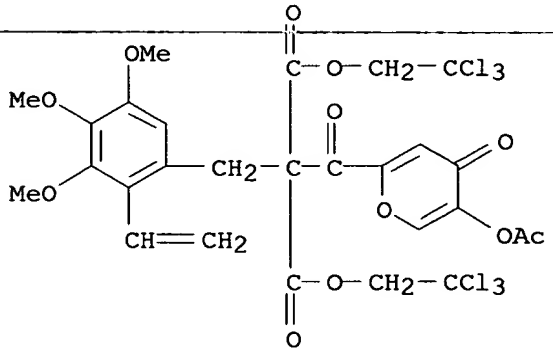
RN 87057-53-2 CAPLUS
CN Propanedioic acid, [(2-ethenylphenyl)methyl][(5-hydroxy-4-oxo-4H-pyran-2-yl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 149295-99-8 CAPLUS
CN Propanedioic acid, [[5-(acetyloxy)-4-oxo-4H-pyran-2-yl]carbonyl][(2-ethenyl-3,4,5-trimethoxyphenyl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

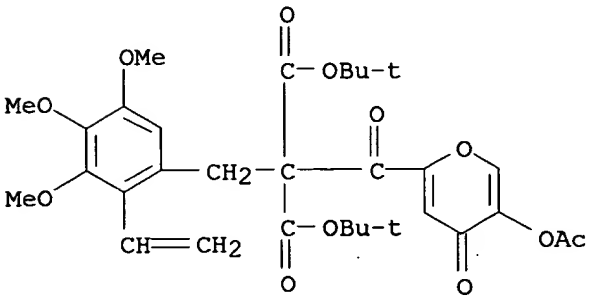


RN 149296-01-5 CAPLUS
CN Propanedioic acid, [[5-(acetyloxy)-4-oxo-4H-pyran-2-yl]carbonyl][(2-ethenyl-3,4,5-trimethoxyphenyl)methyl]-, bis(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)



RN 149296-03-7 CAPLUS

CN Propanedioic acid, [[5-(acetyloxy)-4-oxo-4H-pyran-2-yl]carbonyl][(2-ethenyl-3,4,5-trimethoxyphenyl)methyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

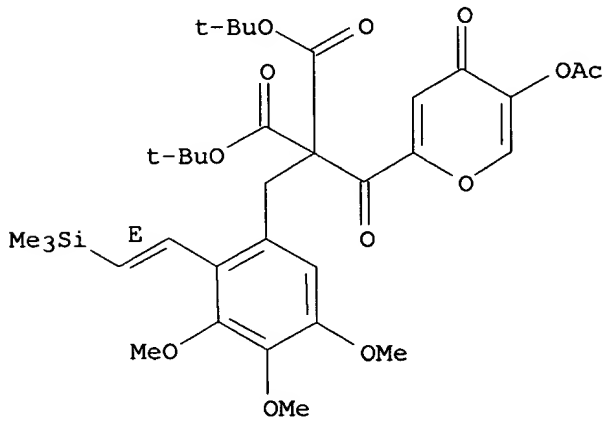


IT **149296-05-9P 149296-06-0P 149296-07-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 149296-05-9 CAPLUS

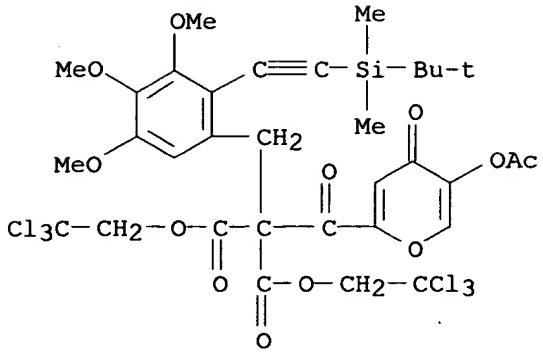
CN Propanedioic acid, [[5-(acetyloxy)-4-oxo-4H-pyran-2-yl]carbonyl][[3,4,5-trimethoxy-2-[2-(trimethylsilyl)ethenyl]phenyl]methyl]-, bis(1,1-dimethylethyl) ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

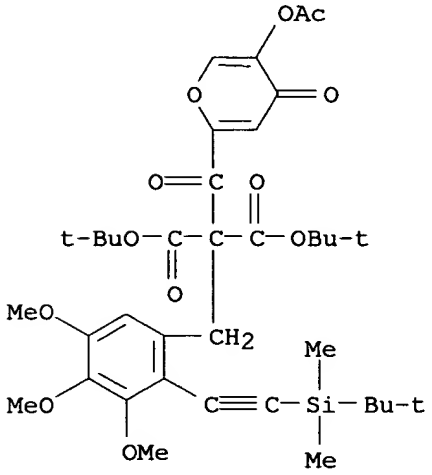


RN 149296-06-0 CAPLUS

CN Propanedioic acid, [[5-(acetyloxy)-4-oxo-4H-pyran-2-yl]carbonyl][[2-[[(1,1-dimethylethyl)dimethylsilyl]ethynyl]-3,4,5-trimethoxyphenyl]methyl]-, bis(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)



RN 149296-07-1 CAPLUS
CN Propanedioic acid, [[5-(acetyloxy)-4-oxo-4H-pyran-2-yl]carbonyl][[2-[[(1,1-dimethylethyl)dimethylsilyl]ethynyl]-3,4,5-trimethoxyphenyl]methyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



L5 ANSWER 12 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:73665 CAPLUS
DN 118:73665
TI Use of angiotensin II receptor antagonists in the treatment of diabetic nephropathy
IN Hill, James
PA Smithkline Beecham PLC, UK
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9210182	A1	19920625	WO 1991-GB2220	19911212 <--
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				

	AU 9190585	A1	19920708	AU 1991-90585	19911212 <--
	EP 561939	A1	19930929	EP 1992-901222	19911212 <--
	EP 561939	B1	19980218		
	R: BE, CH, DE, FR, GB, IT, LI, NL				
	JP 06503343	T2	19940414	JP 1992-502130	19911212 <--
	JP 3512793	B2	20040331		
	US 6028091	A	20000222	US 1999-371673	19990810
PRAI	GB 1990-27210	A	19901214		
	WO 1991-GB2220	W	19911212		
	US 1995-375028	B1	19950119		
	US 1995-535796	B1	19950928		
	US 1996-732027	B1	19961016		
	US 1997-901460	B1	19970728		
	US 1999-277922	B1	19990329		

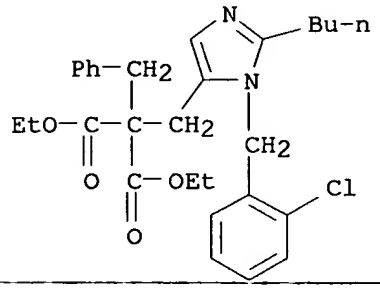
OS MARPAT 118:73665

AB Angiotensin II receptor antagonists (e.g. imidazole derivs.) are used in the manufacture of a medicament for treating diabetic nephropathy. Preparation of 3-[2-n-butyl-1-{(2-chlorophenyl)methyl}-1H-imidazol-5-yl]-2-benzylpropanoic acid and 3 other compds. is described. An injection preparation was made from (E)-3-[2-n-butyl-1-{(4-carboxyphenyl)methyl}-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 50 mg in 25 mL normal saline.

IT **141771-33-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in angiotensin II receptor antagonist preparation for diabetic nephropathy treatment)

RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 13 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:605225 CAPLUS

DN 117:205225

TI Use of angiotensin II receptor antagonists for the preparation of a medicament for improving cognitive function

IN Hill, James

PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9210186	A1	19920625	WO 1991-GB2224	19911212	<--
	W: AU, CA, JP, KR, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE					
	AU 9190692	A1	19920708	AU 1991-90692	19911212	<--
	EP 561896	A1	19930929	EP 1992-900687	19911212	<--
	R: BE, CH, DE, FR, GB, IT, LI, NL					
	JP 06503338	T2	19940414	JP 1992-501731	19911212	<--
	US 2002055490	A1	20020509	US 2001-794723	20010227	
	US 2003096851	A1	20030522	US 2002-287955	20021105	
	US 2003187044	A1	20031002	US 2003-404345	20030401	
PRAI	GB 1990-27197	A	19901214			
	WO 1991-GB2224	A	19911212			
	US 1993-74811	B1	19930610			
	US 1994-325749	B1	19941019			
	US 1995-437000	B1	19950508			
	US 1995-568846	B1	19951207			
	US 1997-835692	B1	19970410			
	US 1998-82010	B1	19980520			
	US 1999-252725	B1	19990219			
	US 1999-371362	B1	19990810			
	US 1999-456868	B1	19991208			
	US 2001-794723	A1	20010227			
	US 2002-287955	B1	20021105			

OS MARPAT 117:205225

AB Angiotensin II receptor antagonists (e.g. imidazole derivs.) are used in the manufacture of a medicament for improving cognitive function. Preparation of 3-[2-n-butyl-1-{(2-chlorophenyl)methyl}-1H-imidazol-5-yl]-2-benzylpropanoic acid and 3 other compds. is described. An injection preparation was made from (E)-3-[2-n-butyl-1-{(4-carboxyphenyl)methyl}-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 50 mg in 25 mL normal saline.

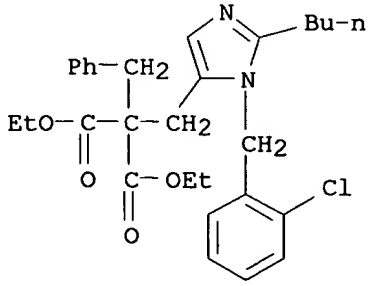
IT **141771-33-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in angiotensin II receptor antagonist preparation for improving cognitive function)

RN 141771-33-7 CAPLUS

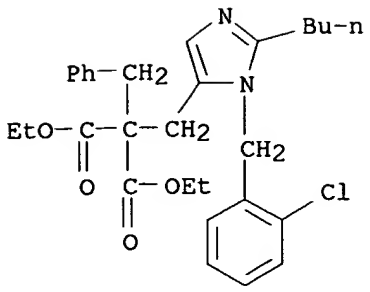
CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 14 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:605208 CAPLUS
DN 117:205208
TI Use of angiotensin II receptor antagonists in the treatment of hemorrhagic stroke
IN Hill, James
PA Smithkline Beecham PLC, UK
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9210188	A1	19920625	WO 1991-GB2226	19911212	<--
	W: AU, CA, JP, KR, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE					
	AU 9190841	A1	19920708	AU 1991-90841	19911212	<--
	EP 561977	A1	19930929	EP 1992-901997	19911212	<--
	EP 561977	B1	20040526			
	R: BE, CH, DE, FR, GB, IT, LI, NL					
	JP 06503558	T2	19940421	JP 1992-501019	19911212	<--
	US 2001018448	A1	20010830	US 2001-805474	20010313	
	US 2002086893	A1	20020704	US 2001-911906	20010724	
	US 2003050285	A1	20030313	US 2002-246872	20020919	
PRAI	GB 1990-27199	A	19901214			
	WO 1991-GB2226	A	19911212			
	US 1993-74807	B1	19930610			
	US 1994-304904	B1	19940913			
	US 1996-614226	B1	19960312			
	US 1997-775344	B1	19970103			
	US 1997-940768	B1	19970930			
	US 1998-153527	B1	19980915			
	US 1999-272775	B1	19990329			
	US 2000-603719	B1	20000627			
	US 2001-805474	A1	20010313			
	US 2001-911906	A1	20010724			

OS MARPAT 117:205208
AB Angiotensin II receptor antagonists (e.g. imidazole derivs.) are used in the manufacture of a medicament for treating hemorrhagic stroke. 5-Bromo-2-n-butyl-1-(2-chlorophenyl)methyl-1H-benzimidazole-7-carboxylic acid was prepared in 4 steps from 2,5-dibromobenzoic acid. Capsules contain (E)-3-[2-n-butyl-1-[(4-carboxyphenyl)methyl]-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg.
IT **141771-33-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in angiotensin II receptor antagonist preparation
for hemorrhagic stroke treatment)
RN 141771-33-7 CAPLUS
CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 15 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:605207 CAPLUS
DN 117:205207
TI Use of angiotensin II antagonists in the treatment of angina pectoris
IN Hill, James
PA Smithkline Beecham PLC, UK
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9210187	A1	19920625	WO 1991-GB2225	19911212 <--
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	AU 9190816	A1	19920708	AU 1991-90816	19911212 <--
	EP 561979	A1	19930929	EP 1992-902007	19911212 <--
	R: BE, CH, DE, FR, GB, IT, LI, NL				
	JP 06503323	T2	19940414	JP 1992-501018	19911212 <--
	US 2001016594	A1	20010823	US 2001-788966	20010220
	US 2001051615	A1	20011213	US 2001-909428	20010719
	US 2002058686	A1	20020516	US 2001-981042	20011016
	US 2002132840	A1	20020919	US 2002-100248	20020315
PRAI	GB 1990-27198	A	19901214		
	WO 1991-GB2225	A	19911212		
	US 1994-286158	B1	19940804		
	US 1996-646175	B1	19960507		
	US 1997-795843	B1	19970206		
	US 1998-39656	B1	19980316		
	US 1999-261893	B1	19990303		
	US 1999-395833	B1	19990914		
	US 2000-499864	B1	20000207		
	US 2000-604450	A1	20000627		
	US 2001-788966	A1	20010220		
	US 2001-909428	A1	20010719		
	US 2001-981042	A1	20011016		

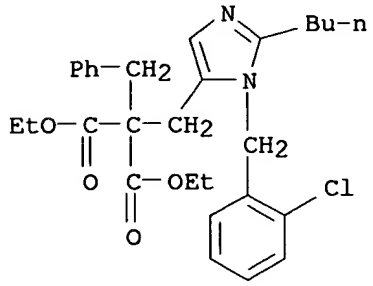
OS MARPAT 117:205207
AB Angiotensin II receptor antagonists (e.g. imidazole derivs.) are used in the manufacture of a medicament for treating angina pectoris. Preparation of 3-[2-n-butyl-1-{(2-chlorophenyl)methyl}-1H-imidazol-5-yl]-2-benzylpropanoic acid and 3 other compds. is described. An injection preparation was made from (E)-3-[2-n-butyl-1-{(4-carboxyphenyl)methyl}-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 50 mg in 25 mL normal

saline.

IT **141771-33-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in angiotensin II receptor antagonist preparation
for angina treatment)

RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 16 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:598524 CAPLUS

DN 117:198524

TI Pharmaceutical compositions, preparation and use of angiotensin II receptor antagonists in the treatment of macular degeneration

IN Hill, James

PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9210179	A1	19920625	WO 1991-GB2217	19911212	<--
	W: AU, CA, JP, KR, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE					
	AU 9190652	A1	19920708	AU 1991-90652	19911212	<--
	EP 561905	A1	19930929	EP 1992-900761	19911212	<--
	R: BE, CH, DE, FR, GB, IT, LI, NL					
	JP 06503333	T2	19940414	JP 1992-501726	19911212	<--
	US 6025380	A	20000215	US 1999-324330	19990602	
PRAI	GB 1990-27212	A	19901214			
	WO 1991-GB2217	A	19911212			
	US 1993-74812	B1	19930610			
	US 1995-375029	B1	19950119			
	US 1995-535502	B1	19950928			
	US 1996-724201	B1	19961001			
	US 1997-901472	B1	19970728			
	US 1998-170550	A1	19981013			

OS MARPAT 117:198524

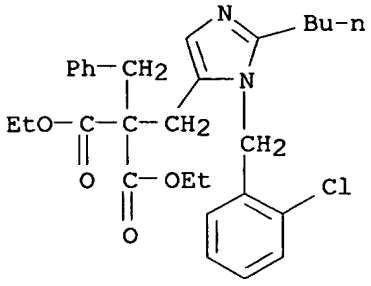
AB Angiotensin II receptor antagonists, e.g. 2-methyl-4-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methoxy]quinoline, are disclosed for the manufacture of a

medicament for the treatment of macular degeneration. Markush are provided, 11 specific compds. are claimed, and preparation of compds. of the invention is described. A capsule contained (E)-3-[2-butyl-1-[(4-carboxyphenyl)methyl]-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg. Tablet and injectable formulations are also given.

IT **141771-33-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, for angiotensin II antagonist preparation for macular degeneration treatment)

RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 17 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:598523 CAPLUS

DN 117:198523

TI Pharmaceutical compositions, preparation and use of angiotensin II antagonist for the treatment of infarction

IN Hill, James

PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9210180	A1	19920625	WO 1991-GB2218	19911212 <--
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	AU 9190529	A1	19920708	AU 1991-90529	19911212 <--
	EP 561878	A1	19930929	EP 1992-900446	19911212 <--
	R: BE, CH, DE, FR, GB, IT, LI, NL				
	JP 06503322	T2	19940414	JP 1992-501017	19911212 <--
	US 2001034360	A1	20011025	US 2001-847120	20010502
	US 2002068759	A1	20020606	US 2001-21321	20011212
	US 2002160985	A1	20021031	US 2002-134894	20020429
	US 2003069293	A1	20030410	US 2002-271177	20021015
PRAI	GB 1990-27208	A	19901214		
	WO 1991-GB2218	A	19911212		
	US 1993-74809	B1	19930610		
	US 1994-303785	B1	19940909		

	US 1995-434144	B1	19950502
	US 1996-588826	B1	19960119
	US 1996-740382	B1	19961029
	US 1997-932418	B1	19970917
	US 1998-158431	B1	19980921
	US 1999-255986	B1	19990223
	US 1999-344782	B1	19990625
	US 1999-431896	B1	19991102
	US 2000-539125	B1	20000330
	US 2000-679149	B1	20001005
	US 2001-847120	B1	20010502
	US 2001-969707	A1	20011003
	US 2001-21321	A1	20011212
	US 2002-134894	A1	20020429

OS MARPAT 117:198523

AB Angiotensin II receptor antagonists, e.g. 2-methyl-4-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methoxy]quinoline, are disclosed for the manufacture of a medicament for the treatment of infarction. Markush are provided, 11 specific compds. are claimed, and preparation of compds. of the invention is described. A capsule formulation contained (E)-3-[2-butyl-1-((4-carboxyphenyl)methyl)-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg. Tablet and injectable formulations are also given.

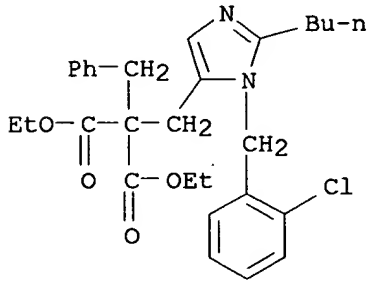
IT **141771-33-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, for angiotensin II antagonist preparation for infarction treatment)

RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 18 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:598522 CAPLUS

DN 117:198522

TI Pharmaceutical compositions, preparation and use of angiotensin II antagonists in the treatment of left ventricular hypertrophy

IN Hill, James

PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9210181	A1	19920625	WO 1991-GB2219	19911212 <--
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	AU 9190712	A1	19920708	AU 1991-90712	19911212 <--
	JP 06503334	T2	19940414	JP 1992-501727	19911212 <--
	EP 660713	A1	19950705	EP 1992-900691	19911212 <--
	EP 660713	B1	20011024		
	R: BE, CH, DE, FR, GB, IT, LI, NL				
	US 6034114	A	20000307	US 1999-371363	19990810
PRAI	GB 1990-27209	A	19901214		
	WO 1991-GB2219	A	19911212		
	US 1993-281250	B1	19930330		
	US 1995-375016	B1	19950119		
	US 1995-534899	B1	19950928		
	US 1996-732078	B1	19961016		
	US 1997-902560	B1	19970728		
	US 1998-170560	B1	19981013		

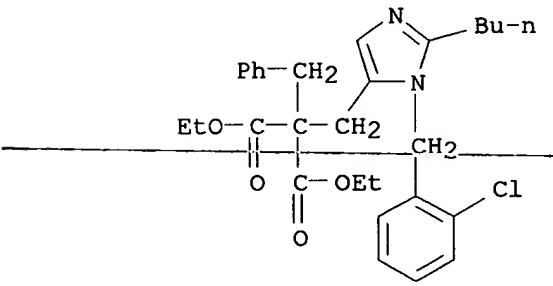
OS MARPAT 117:198522

AB Angiotensin II receptor antagonists (Markush included) are provided for the manufacture of a medicament for the treatment of left ventricular hypertrophy regression. Synthesis of representative compds. is included, and 11 specific compds. are claimed. A capsule formulation contained (E)-3-[2-n-butyl-1-((4-carboxyphenyl)methyl)-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg. Tablet and injectable formulations are also presented.

IT **141771-33-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, for angiotensin II antagonist preparation for left
ventricular hypertrophy regression treatment)

RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 19 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:598521 CAPLUS

DN 117:198521

TI Pharmaceutical compositions, preparation and use of angiotensin II receptor antagonists for the prevention of restenosis

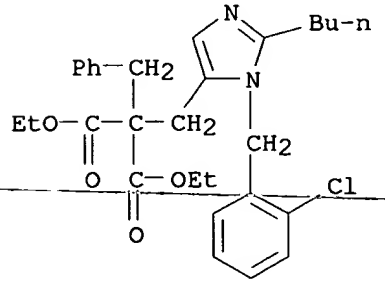
IN Hill, James

PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9210185	A1	19920625	WO 1991-GB2223	19911212 <--
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	AU 9190691	A1	19920708	AU 1991-90691	19911212 <--
	EP 561895	A1	19930929	EP 1992-900686	19911212 <--
	R: BE, CH, DE, FR, GB, IT, LI, NL				
	JP 06503337	T2	19940414	JP 1992-501730	19911212 <--
	US 5387601	A	19950207	US 1993-74810	19930610 <--
PRAI	GB 1990-27200	A	19901214		
	WO 1991-GB2223	A	19911212		

OS MARPAT 117:198521
AB Angiotensin II receptor antagonists, e.g. 2-methyl-4-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methoxy]quinoline, are disclosed for the manufacture of a medicament for the prevention of restenosis after angioplasty or bypass surgery. Markush are provided, 11 specific compds. are claimed, and preparation of compds. of the invention is described. A capsule formulation contained (E)-3-[2-butyl-1-((4-carboxyphenyl)methyl)-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg. Tablet and injectable formulations are also given.
IT **141771-33-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, for angiotensin II antagonist preparation for restenosis prevention)
RN 141771-33-7 CAPLUS
CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 20 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:598520 CAPLUS
DN 117:198520
TI Pharmaceutical compositions, preparation and use of angiotensin II receptor antagonists for the treatment of atheroma
IN Hill, James
PA Smithkline Beecham PLC, UK
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9210184	A1	19920625	WO 1991-GB2222	19911212	<--
	W: AU, CA, JP, KR, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE					
	AU 9190641	A1	19920708	AU 1991-90641	19911212	<--
	EP 561876	A1	19930929	EP 1992-900436	19911212	<--
	EP 561876	B1	19970312			
	R: BE, CH, DE, FR, GB, IT, LI, NL					
	JP 06503336	T2	19940414	JP 1992-501729	19911212	<--
	US 2002006949	A1	20020117	US 2001-795507	20010227	
	US 2003004201	A1	20030102	US 2002-134920	20020429	
	US 2003166700	A1	20030904	US 2003-379137	20030304	
PRAI	GB 1990-27201	A	19901214			
	WO 1991-GB2222	A	19911212			
	US 1994-325731	B1	19941019			
	US 1995-568919	B1	19951207			
	US 1997-798671	B1	19970211			
	US 1997-987288	B1	19971209			
	US 1998-162404	B1	19980928			
	US 1999-339303	B1	19990623			
	US 1999-456870	B1	19991208			
	US 2000-592492	A1	20000612			
	US 2001-795507	B1	20010227			
	US 2001-955398	A1	20010918			
	US 2002-134920	B1	20020429			

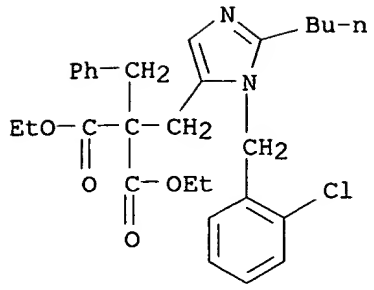
OS MARPAT 117:198520

AB Angiotensin II receptor antagonists, e.g. 2-methyl-4-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methoxy]quinoline, are disclosed for the manufacture of a medicament for the treatment of atheroma. Markush are provided, 11 specific compds. are claimed, and preparation of compds. of the invention is described. A capsule formulation contained (E)-3-[2-butyl-1-((4-carboxyphenyl)methyl)-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg. Tablet and injectable formulations are also given.

IT **141771-33-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, for angiotensin II antagonist preparation for atheroma treatment)

RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)

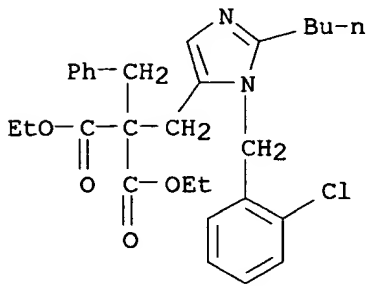


L5 ANSWER 21 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:598519 CAPLUS
DN 117:198519
TI Pharmaceutical compositions, preparation and use of angiotensin II receptor antagonists in the treatment of diabetic retinopathy
IN Hill, James
PA Smithkline Beecham PLC, UK
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9210183	A1	19920625	WO 1991-GB2221	19911212 <--
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	AU 9190649	A1	19920708	AU 1991-90649	19911212 <--
	EP 561901	A1	19930929	EP 1992-900718	19911212 <--
	R: BE, CH, DE, FR, GB, IT, LI, NL				
	JP 06503335	T2	19940414	JP 1992-501728	19911212 <--
	US 2002128300	A1	20020912	US 2001-929814	20010814
PRAI	GB 1990-27211	A	19901214		
	WO 1991-GB2221	A	19911212		
	US 1993-74869	B1	19930610		
	US 1994-237461	B1	19940503		
	US 1995-388781	B1	19950215		
	US 1996-598760	B1	19960321		
	US 1997-835693	B1	19970410		
	US 1998-48708	B1	19980326		
	US 1999-233689	B1	19990119		
	US 1999-456867	B1	19991208		
	US 2000-592492	A1	20000612		
	US 2000-592495	B1	20000612		
	US 2001-795021	A1	20010227		

OS MARPAT 117:198519
AB Angiotensin II receptor antagonists, e.g. 2-methyl-4-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methoxy]quinoline, are disclosed for the manufacture of a medicament for the treatment of diabetic retinopathy, Markush are provided, 11 specific compds. are claimed, and preparation of compds. of the invention is described. A capsule formulation contained (E)-3-[2-butyl-1-((4-carboxyphenyl)methyl)-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg. Tablet and injectable formulations are also given.

IT **141771-33-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, for angiotensin II antagonist preparation for diabetic retinopathy treatment)
RN 141771-33-7 CAPLUS
CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 22 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:578319 CAPLUS
DN 117:178319
TI Antihypertensive compositions containing diuretics and angiotensin II receptor antagonists
IN Weinstock, Joseph
PA SmithKline Beckman Corp., USA
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9210097	A1	19920625	WO 1991-US9362	19911213	<--
	W: AU, CA, JP, KR, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE					
	CA 2098176	AA	19920614	CA 1991-2098176	19911213	<--
	AU 9191782	A1	19920708	AU 1991-91782	19911213	<--
	AU 656551	B2	19950209			
	EP 565634	A1	19931020	EP 1992-904382	19911213	<--
	EP 565634	B1	19990317			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE					
	JP 06503834	T2	19940428	JP 1992-504315	19911213	<--
	JP 3398379	B2	20030421			
	AT 177634	E	19990415	AT 1992-904382	19911213	
	ES 2130170	T3	19990701	ES 1992-904382	19911213	
	US 5656650	A	19970812	US 1995-444121	19950518	<--
	HK 1012209	A1	20000512	HK 1998-113489	19981215	
PRAI	US 1990-628807	A2	19901214			
	WO 1991-US9362	A	19911213			
	US 1993-75535	A1	19930610			

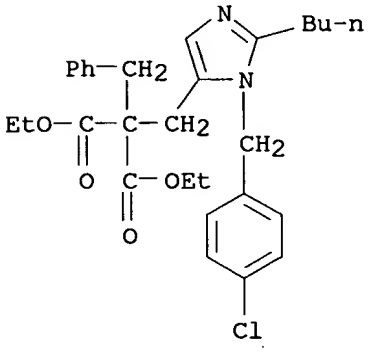
OS MARPAT 117:178319
AB A pharmaceutical composition contains an angiotensin II receptor antagonist and a compound selected from a diuretic, a Ca channel blocker, a

β-adrenoreceptor blocker, a renin inhibitor, and an angiotensin-converting enzyme inhibitor for the treatment of hypertension. A capsule contained (E)-3-[2-butyl-1-{(4-carboxyphenyl)-thienyl)-methyl-2-propenoic acid (I) 100, and hydrochlorothiazide (II) 50mg. II enhanced the hypotensive efficacy of I. Imidazole derivs. (Markush given) as angiotensin II receptor antagonists were prepared

IT **143851-89-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of angiotensin II receptor antagonist)

RN 143851-89-2 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(4-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 23 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:571061 CAPLUS

DN 117:171061

TI A practical method for the oxidative coupling of aromatic compounds

AU Tanaka, Masahide; Mitsuhashi, Hiroshi; Wakamatsu, Takeshi

CS Tsumura Res. Inst. Biol. Chem., Ami, 300-11, Japan

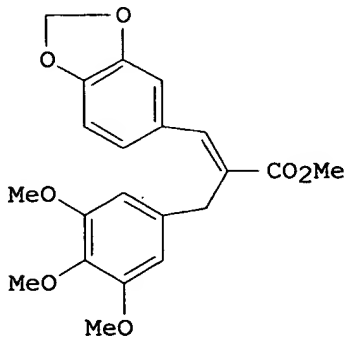
SO Tetrahedron Letters (**1992**), 33(29), 4161-4
CODEN: TELEAY; ISSN: 0040-4039

DT Journal

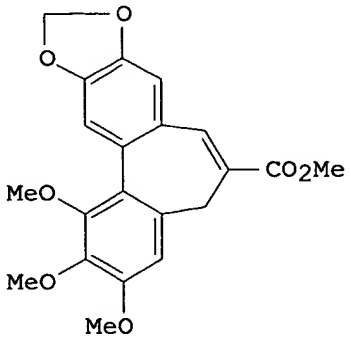
LA English

OS CASREACT 117:171061

GI



I



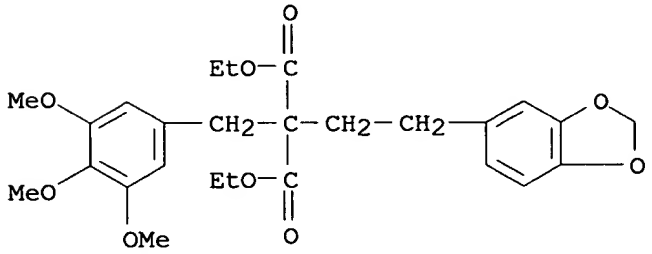
II

AB A practical method for the oxidative coupling reaction of phenolic and nonphenolic compds. is described. The versatility of this reaction was demonstrated by the successful coupling of the wide variety of substrates including catecholic compds. and known intermediates for the synthesis of steganacin and its analogs. Thus intramol. coupling of diphenylpropene I in the presence of Fe(ClO4)3 in CF3CO2H/CH2Cl2 gave 85% dibenzocycloheptene II.

IT **58745-52-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidative coupling reaction of, in the presence of iron perchlorate, dibenzocyclooctane from)

RN 58745-52-1 CAPLUS

CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(3,4,5-trimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 24 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:407921 CAPLUS

DN 117:7921

TI Preparation of imidazolylalkanoates as angiotensin II antagonists

IN Girard, Gerald Robert; Hempel, Judith; Hill, David Taylor; Samanen, James; Weinstock, Joseph

PA SmithKline Beecham Corp., USA

SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2

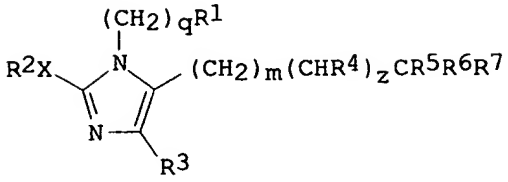
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9202510	A1	19920220	WO 1991-US5391	19910730	<--
	W: AU, CA, JP, KR, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE					
	CA 2087840	AA	19920201	CA 1991-2087840	19910730	<--
	AU 9184931	A1	19920302	AU 1991-84931	19910730	<--
	AU 649270	B2	19940519			
	ZA 9105962	A	19920729	ZA 1991-5962	19910730	<--
	EP 541705	A1	19930519	EP 1991-915339	19910730	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
	JP 05509106	T2	19931216	JP 1991-514483	19910730	<--
	US 5444080	A	19950822	US 1993-965291	19930129	<--
	US 5530017	A	19960625	US 1995-433001	19950502	<--
PRAI	US 1990-560643	A2	19900731			
	WO 1991-US5391	A	19910730			

US 1993-965291 A3 19930129
OS MARPAT 117:7921
GI



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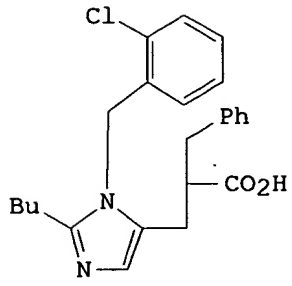
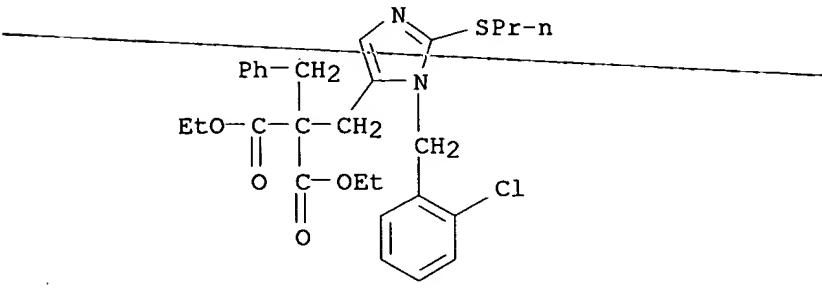


II

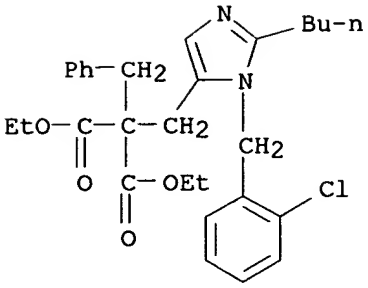
AB Title compds. [I; R1 = adamantylmethyl, (substituted) Ph, biphenyl, naphthyl; R2 = alkyl, alkenyl, alkynyl cycloalkyl, (substituted) Ph; R3 = H, Cl, Br, F, iodo, CHO, HOCH2, CO2R8, NO2, F3C, C2F5, F3CCF2CF2; R4 = H, alkyl; R5 = alkyl, alkenyl, (substituted) phenyl(alkyl), thienyl(alkyl), furyl(alkyl), pyridyl(alkyl), tetrazolyl(alkyl), etc.; R6 = CO2R8, CONR8R8, tetrazol-5-yl; R7 = H, CO2R8, alkyl; R8 = H, alkyl, (methyl)phenyl; X = bond, S, O; m = 0-2; q = 0-4; z = 0-1] are prepared as angiotensin II antagonists (no data). Thus, 2-butyl-1-(2-chlorophenyl)methyl-5-chloromethyl-1H-imidazole (preparation from imidazole given) was condensed with di-Et benzylmalonate using NaH in DMF to give 85% coupling product, which was refluxed with aqueous KOH followed by acidification with HCl to give title compound II. Capsules were prepared containing II.

IT **141771-32-6P 141771-33-7P 141771-44-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for imidazolylalkanoate angiotensin II antagonist)

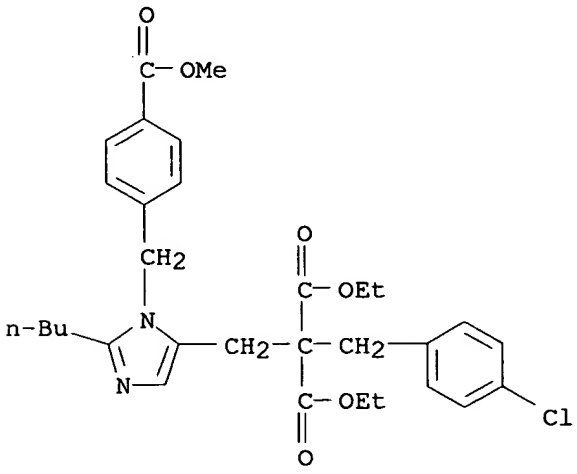
RN 141771-32-6 CAPLUS
CN Propanedioic acid, [[1-[(2-chlorophenyl)methyl]-2-(propylthio)-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



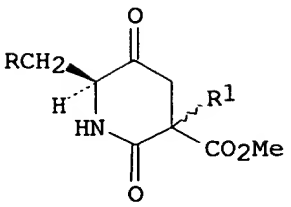
RN 141771-33-7 CAPLUS
CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 141771-44-0 CAPLUS
CN Propanedioic acid, [[2-butyl-1-[[4-(methoxycarbonyl)phenyl]methyl]-1H-imidazol-5-yl]methyl][(4-chlorophenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 25 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:256027 CAPLUS
DN 116:256027
TI Synthesis of cyclic ketomethylene dipeptide derivatives
AU Dominguez, M. J.; Gonzalez-Muniz, R.; Garcia-Lopez, M. T.
CS Inst. Quim. Med., Madrid, 28006, Spain
SO Tetrahedron (**1992**), 48(13), 2761-72
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
OS CASREACT 116:256027
GI



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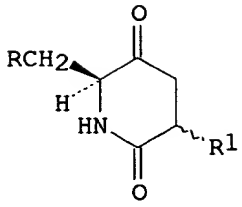


II

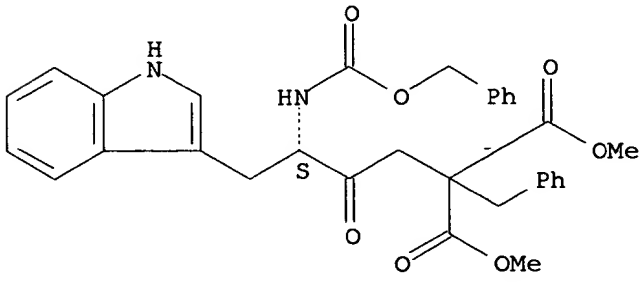
AB Me 6-aralkyl-2,5-diketopiperidine-3-carboxylates I (R = Ph, 3-indolyl; R1 = H) derived from L-Phe and L-Trp, and their 3-substituted analogs I (R = Ph, 3-indolyl; R1 = CH2Ph, CO2CO2Et, Me) in which the 3-substituent is the side chain of Phe, Asp, and Ala have been synthesized. Cyclo[Trpψ(COCH2)Gly] (II; R = 3-indolyl, R1 = H) and cyclo[Pheψ(COCH2)-ξ-Phe] (II; R = Ph, R1 = CH2Ph) have been also prepared

IT **141672-16-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, deblocking, and cyclization of, piperidinedione from)

RN 141672-16-4 CAPLUS

CN Propanedioic acid, [4-(1H-indol-3-yl)-2-oxo-3-[[(phenylmethoxy)carbonyl]amino]butyl](phenylmethyl)-, dimethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 26 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1990:56713 CAPLUS

DN 112:56713

TI Preparation of N-acyl-L-histidinamide derivatives as renin inhibitors

PA Fujisawa Pharmaceutical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF

DT Patent

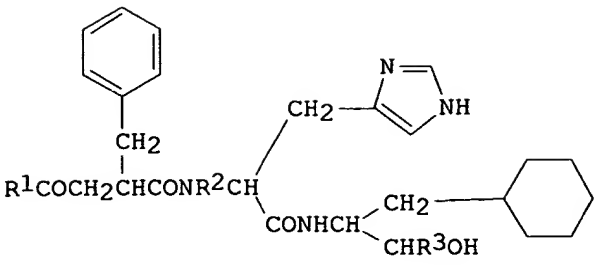
LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 01131162	A2	19890524	JP 1988-259897	19881014 <--
PRAI GB 1987-24428	A	19871019		

OS MARPAT 112:56713

GI



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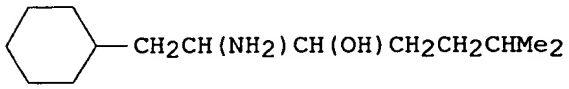
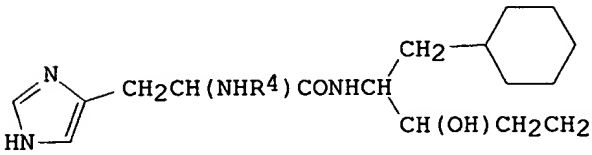


II



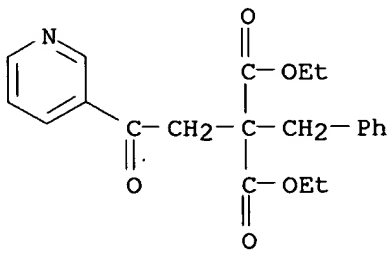
III

AB Amino acid derivs. [I; R1 = (substituted) aryl, alkyl, heterocyclyl; R2 = H, alkyl; R3 = alkyl], effective renin inhibitors useful as antihypertensives, are prepared Ph2P(O)N3 (390 mg) and 144 mg Et3N were added to a solution of 363 mg BOC-His-OH (BOC= tert-BuO2C) and 294 mg (2S,3S)-II in DMF at 0° and stirred overnight at 25° to give 384 mg (2S,3S)-III (R4 = BOC) which was deprotected with CF3CO2H to give 275 mg (2S,3S)-III (R4 = H) (IV). Ph2P(O)N3 (0.75 g) and 0.28 g Et3N were added to a solution of 0.74 g PhCOCH2CH(CO2H)CH2Ph and 1.00 g IV in DMF under ice cooling and the solution stirred overnight at room temperature to give 1.21 g diastereomeric (2S,3S)-I (R1 = Ph, R2 = H, R3 = Me2CHCH2CH2) which was separated by silica gel thin-layer chromatog. Also prepared were 6 addnl. I, 3 of which showed plasma renin inhibitory activity with IC50 of 4.5, 7.9, and 9.5 + 10-8M.

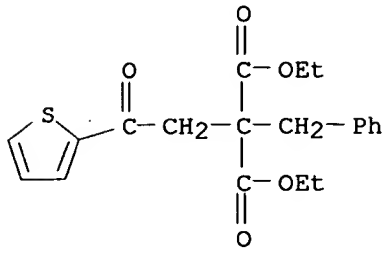
IT **124640-86-4P 124640-89-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of renin inhibitor)

RN 124640-86-4 CAPLUS

CN Propanedioic acid, [2-oxo-2-(3-pyridinyl)ethyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 124640-89-7 CAPLUS
CN Propanedioic acid, [2-oxo-2-(2-thienyl)ethyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)

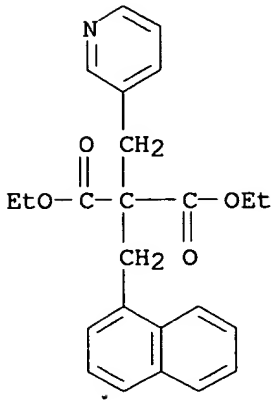


L5 ANSWER 27 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1988:94949 CAPLUS
DN 108:94949
TI Preparation of statine-containing peptides as orally-active renin inhibitors
IN Morisawa, Yasuhiro; Yabe, Yuichiro; Kataoka, Mitsuru; Iijama, Yasuteru; Koike, Hiroyuki; Takahagi, Hidekuni; Kokubu, Tatsuo; Hiwada, Kunio
PA Sankyo Co., Ltd. , Japan
SO Eur. Pat. Appl., 112 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

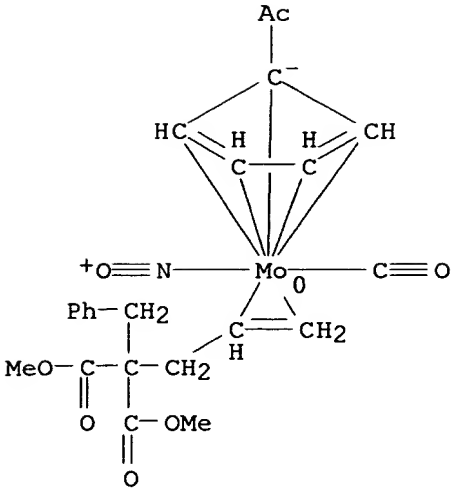
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 228192	A2	19870708	EP 1986-309362	19861201	<--
	EP 228192	A3	19890823			
	R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE					
	JP 62142145	A2	19870625	JP 1985-268415	19851129	<--
	JP 06062530	B4	19940817			
	JP 63063649	A2	19880322	JP 1986-208621	19860904	<--
	JP 07020918	B4	19950308			
	JP 62246546	A2	19871027	JP 1986-307058	19861223	<--
	JP 07049405	B4	19950531			
PRAI	JP 1985-268415	A	19851129			
	JP 1985-297664	A	19851226			
	JP 1986-208621	A	19860904			

OS CASREACT 108:94949
AB R1R2CHCONR3CHR4CONHCH(CH2R5)CH(OH)(CH2)nCONH(CHR6CONH)nR7 [I; R1 = arylalkyl, heterocyclylalkyl, acylalkyl, alkoxyalkoxyalkyl, (substituted) carbamoyl, acylamino; R2 = arylalkyl, heterocyclyalkyl; R3 = H, alkyl; R4 = H, (substituted) alkyl, haloalkenyl, alkynyl, cycloalkyl; R5 = Me2CH, cycloalkyl, Ph; R6 = alkyl; R7 = (substituted) alkyl; m, n = 0, 1] were prepared as renin inhibitors. N-Nicotinoyl-3-(1-naphthyl)-L-alanyl-L-leucylstatyl-L-lysinol.HCl was prepared via solution-phase method using (EtO)2P(O)CN/Et3N in DMF. I gave 68-98% inhibition of human renin at 10-6M.
IT **112804-18-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as renin inhibitor intermediate)
RN 112804-18-9 CAPLUS

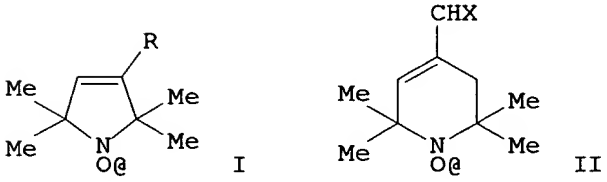
CN Propanedioic acid, (1-naphthalenylmethyl)(3-pyridinylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)

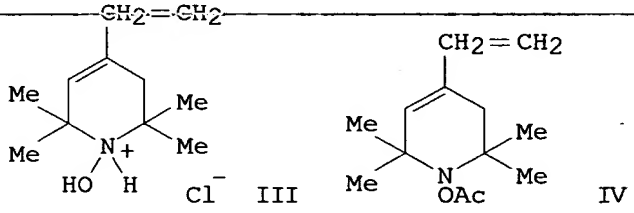


L5 ANSWER 28 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1987:617788 CAPLUS
DN 107:217788
TI Acetyl substitution of the cyclopentadienyl ligand in molybdenum complexes; nucleophilic additions to coordinated allyl groups
AU Vanarsdale, W. E.; Kochi, J. K.
CS Dep. Chem., Univ. Houston, Houston, TX, 77004, USA
SO Journal of Organometallic Chemistry (**1986**), 317(2), 215-32
CODEN: JORCAI; ISSN: 0022-328X
DT Journal
LA English
OS CASREACT 107:217788
AB Reaction of ClMoL(CO)2(NCMe)2 (I; L = η3-allyl, η3-CH2CHCHMe, η3-CHCMeCH2) with CpLi (Cp = η5-cyclopentadienyl) gave CpMoL(CO)2 (same L) and <10% (AcCp)MoL(CO)2 (II). II (same L) were also prepared in 50-60% yields by treating I with lithiated acetylcyclopentadiene. The origin of the Ac group was determined by D labeling, and is rationalized in terms of activation of the coordinated MeCN to nucleophilic addition with CpLi. The x-ray crystal structure of II (L = η3-allyl) showed a slightly distorted Cp ring and an effective enlargement of the ligand as a result of Ac substitution. Stereoelectronic consequences of the AcCp ligand are found in the relative populations of the exo and endo conformations of the coordinated allyl ligands in both II and (AcCp)Mo(CO)(NO)(η3-allyl)+ (III) by comparison with their unsubstituted analogs. The stereochem. resulting from this steric change is also examined in nucleophilic addns. to III with H-, thiolate anions, and carbanions.
IT **111194-27-5P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and rotamers of)
RN 111194-27-5 CAPLUS
CN Molybdenum, [(1,2,3,4,5-η)-1-acetyl-2,4-cyclopentadien-1-yl]carbonyl[dimethyl (phenylmethyl)[(2,3-η)-2-propenyl]propanedioate]nitrosyl- (9CI) (CA INDEX NAME)



L5 ANSWER 29 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1987:423206 CAPLUS
DN 107:23206
TI Further syntheses with nitroxide α,β-unsaturated aldehydes and allylic bromides
AU Hideg, Kalman; Cseko, Jozsef; Hankovszky, H. Olga; Sohar, Pal
CS Cent. Lab. Chem., Univ. Pecs, Pecs, H-7643, Hung.
SO Canadian Journal of Chemistry (**1986**), 64(8), 1482-90
CODEN: CJCHAG; ISSN: 0008-4042
DT Journal
LA English
OS CASREACT 107:23206
GI





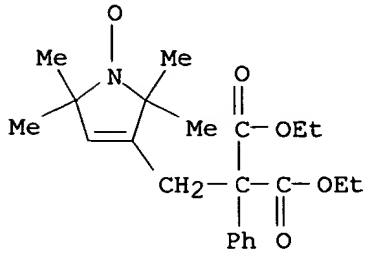
AB The enhanced reactivity of nitroxide allylic bromides, e.g. I (R = CH2Br), is used for preparation of spin-labeled analogs of biol. active compds. (morphine, Nalorphine, barbituric acid, choline and acetyl choline). Thus, I (R = CH2Br) was treated with Me2NCH2CH2OAc to give 45% I (R =

CH2N+Me2CH2CH2OAc Br-). Nitroxide α,β-unsatd. aldehydes, e.g. II (X = O), are reacted with phosphoranes to give nitroxide polyenes, e.g. II (X = CH2). The nitroxides are reduced to diamagnetic N-hydroxy hydrochloride salts, e.g. III, which can be converted in the presence of base to N-acetoxy derivs., e.g. IV.

IT **105843-26-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 105843-26-3 CAPLUS

CN 1H-Pyrrol-1-yloxy, 3-[3-ethoxy-2-(ethoxycarbonyl)-3-oxo-2-phenylpropyl]-2,5-dihydro-2,2,5,5-tetramethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 30 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1987:19056 CAPLUS

DN 106:19056

TI 5-Amino-4-hydroxyvaleramide derivatives.

IN Buehlmayer, Peter; Rasetti, Vittorio; Fuhrer, Walter; Stanton, James Lawrence; Goeschke, Richard

PA Ciba-Geigy A.-G., Switz.

SO Eur. Pat. Appl., 180 pp.
CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 184550	A2	19860611	EP 1985-810523	19851108	<--
	EP 184550	A3	19880120			
	EP 184550	B1	19920318			
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
	US 4727060	A	19880223	US 1985-794914	19851104	<--
	AT 73778	E	19920415	AT 1985-810523	19851108	<--
	FI 8504434	A	19860514	FI 1985-4434	19851111	<--
	DD 239210	A5	19860917	DD 1985-282727	19851111	<--
	DK 8505202	A	19860514	DK 1985-5202	19851112	<--
	NO 8504516	A	19860514	NO 1985-4516	19851112	<--
	AU 8549821	A1	19860522	AU 1985-49821	19851112	<--
	AU 592768	B2	19900125			
	JP 61122296	A2	19860610	JP 1985-252104	19851112	<--
	ZA 8508662	A	19860730	ZA 1985-8662	19851112	<--
	HU 39193	A2	19860828	HU 1985-4327	19851112	<--
	ES 548798	A1	19870501	ES 1985-548798	19851112	<--
	ES 557316	A1	19880401	ES 1987-557316	19870114	<--
	US 4931591	A	19900605	US 1989-380711	19890712	<--
	AU 8943855	A1	19900322	AU 1989-43855	19891027	<--

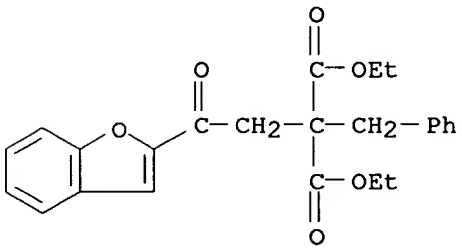
PRAI CH 1984-5426 A 19841113
CH 1985-3094 A 19850717
CH 1983-6285 A 19831123
US 1985-794914 A3 19851104
EP 1985-810523 A 19851108
US 1987-123618 B1 19871228

AB R1-Z-NR2CHR3CHR4CH2CHR5COR6 I [R1 = H, acyl; R2 = H, alkyl; R3 = H, etherified hydroxyalkyl, acyloxyalkyl, cycloalkyl, etc.; R4 = OH, etherified or OH, acyloxy; R5 = alkyl, etherified hydroxyalkyl, acyloxyalkyl, cycloalkyl, etc.; R6 = substituted amino; Z = (N-alkyl) α-amino acid residue], useful as antihypertensives and cardiac stimulants (no data), were prepared Thus, N-(2-quinolylcarbonyl)-L-phenylalanine was condensed with Me2CHCH2CH(NH2)CH(OH)CH2CH(CHMe2)CONHMe in the presence of hydroxybenzotriazole and N,N'-dicyclohexylcarbodiimide to give I [R1 = 2-quinolylcarbonyl, R2 = H, R3 = Me2CHCH2, R4 = OH, R5 = CHMe2, R6 = NHMe, Z = Phe]. Gelatin solns. were prepared from N-[2-(R, S)-benzyl-5,5-dimethyl-4-oxohexanoyl]-His-Cha-cVal-NHBu [Cha = reduced L-cyclohexylalanyl, cVal = CH2CH(CHMe2)CO] 3 mg, gelatin 150.0 mg, phenol 4.7 mg, and water (to 1.0 mL total volume).

IT **105852-56-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of)

RN 105852-56-0 CAPLUS

CN Propanedioic acid, [2-(2-benzofuranyl)-2-oxoethyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 31 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1986:149076 CAPLUS

DN 104:149076

TI Stereoselectivity in carbanion addition to coordinated allyl ligands. Catalytic (exo-endo) isomerization of cationic molybdenum complexes

AU VanArsdale, W. E.; Winter, R. E. K.; Kochi, J. K.

CS Dep. Chem., Univ. Houston, Houston, TX, 77004, USA

SO Organometallics (**1986**), 5(4), 645-55
CODEN: ORGND7; ISSN: 0276-7333

DT Journal

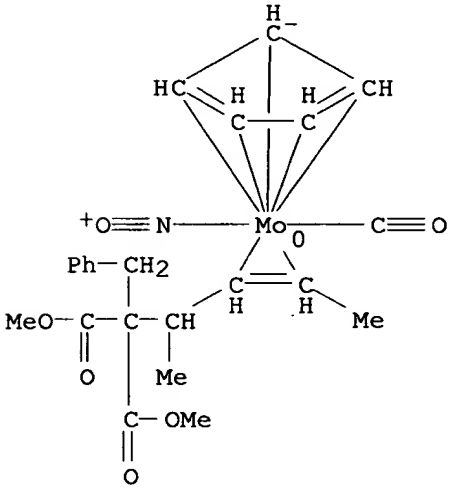
LA English

OS CASREACT 104:149076

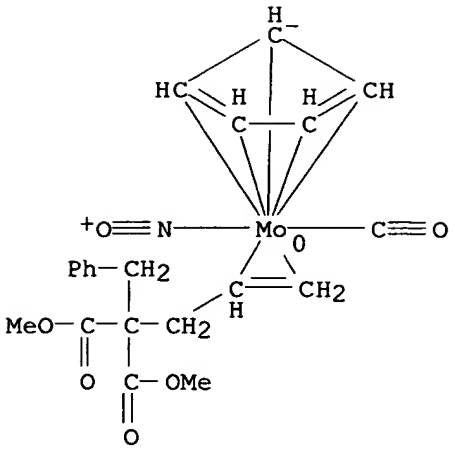
AB Regio- and stereochem. in the nucleophilic addition of various types of carbanions to coordinated allyl ligands is examined in a series of (η5-C5H5)Mo(NO)(CO)(η3-allyl)+ (I). Stereoselectivity is determined primarily by the conformational preference of the allyl ligand in the endo and exo isomers of I. Different additives, including the carbanion itself, induce an efficient catalytic equilibration of the conformational

population which can be faster than nucleophilic addition The rapidity of such a preequil. endo-exo interconversion can lead to a high degree of stereoselectivity in the addition of various carbanionic nucleophiles to I. Thus the η2-olefin product of the addition of the di-Me benzylmalonate anion to the 1,3-dimethallyl cation is a single diastereomer formed in high yields. The stereochem. of the adduct (η5-C5H5)Mo(NO)(CO)(η2-C17H22O4) is established by x-ray crystallog.

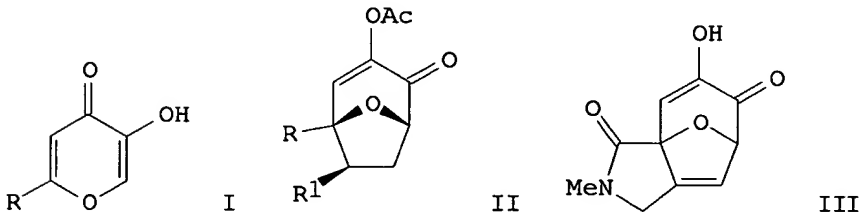
IT **100243-60-5P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystal structure of)
RN 100243-60-5 CAPLUS
CN Molybdenum, carbonyl(η5-2,4-cyclopentadien-1-yl)[dimethyl [(2,3-η)-1-methyl-2-butenyl](phenylmethyl)propanedioate]nitrosyl-, stereoisomer (9CI) (CA INDEX NAME)

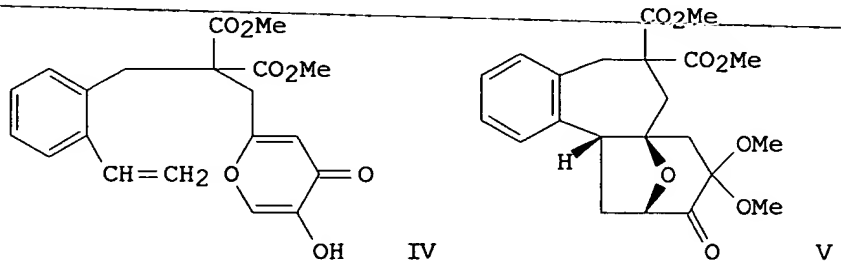


IT **100229-44-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 100229-44-5 CAPLUS
CN Molybdenum, carbonyl(η5-2,4-cyclopentadien-1-yl)[dimethyl (phenylmethyl)[(2,3-η)-2-propenyl]propanedioate]nitrosyl-, stereoisomer (9CI) (CA INDEX NAME)



L5 ANSWER 32 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1983:522228 CAPLUS
DN 99:122228
TI Intramolecular cycloadditions with 2-(ω-alkenyl)-5-hydroxy-4-pyrones
AU Garst, Michael E.; McBride, Bill J.; Douglass, James G., III
CS Dep. Chem., Univ. California, San Diego, CA, 92093, USA
SO Tetrahedron Letters (**1983**), 24(16), 1675-8
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 99:122228
GI





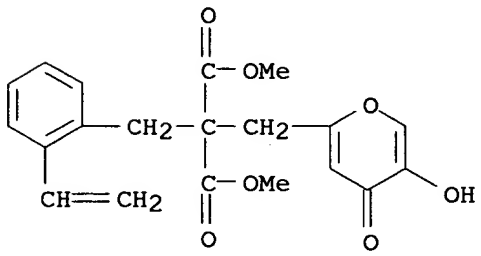
AB The intramol. cycloaddn. reaction of the pyrones I [R = CONMeCH2CH:CH2, CH2C(CO2Me)2(CH2)nCH:CH2 (n = 1, 2)] in refluxing C6H6 for 12-48 h followed by acetylation gave the tricyclic compds. II [RR1 = CONHMeCH2,

CH2C(CO2Me)2(CH2)n (n = 1, 2)], resp., in 55-70% yield. Similarly, cycloaddn. reaction of I (R = CONMeCH2C.tplbond.CH) gave 42% tricyclic compound III. Treatment of pyrone IV with MeSO3H in refluxing MeOH for 12 h gave 87% ketal V.

IT **87057-53-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, intramol. cycloaddn. reaction, and ketalization of)

RN 87057-53-2 CAPLUS

CN Propanedioic acid, [(2-ethenylphenyl)methyl][(5-hydroxy-4-oxo-4H-pyran-2-yl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 33 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1981:139754 CAPLUS

DN 94:139754

TI Synthesis of some pyrazolo [diazepine, pyrazole, isoxazole and pyrimidine] derivatives and related compounds

AU Afsah, El Sayed; Amer, Fathy A.; Soafan, Momdouh

CS Fac. Sci., Mansoura Univ., Mansoura, Egypt

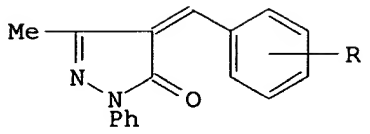
SO Zeitschrift fuer Naturforschung, Teil B: Anorganische Chemie, Organische Chemie (**1980**), 35B(10), 1313-16
CODEN: ZNBAD2; ISSN: 0340-5087

DT Journal

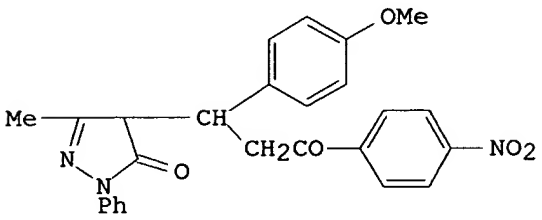
LA English

OS CASREACT 94:139754

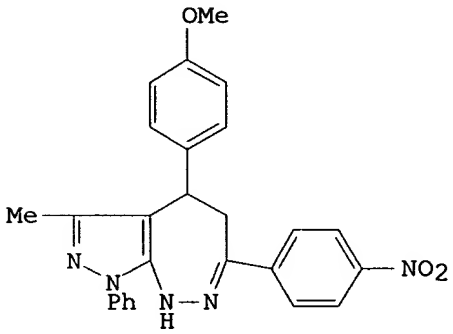
GI



I



II



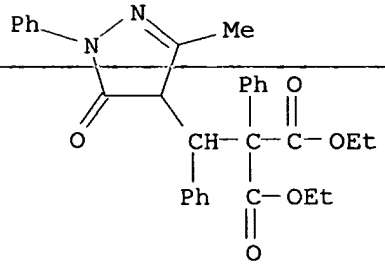
III

AB Eighteen title compds. were prepared in 55-75% yields by various methods starting from I (R = H, o-, p-OH, p-MeO). Thus, Michael condensation of I (R = p-MeO) with p-O2NC6H4Ac gave 75% II, which on cyclization with NH2NH2 gave 60% III.

IT **76794-82-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 76794-82-6 CAPLUS

CN Propanedioic acid, [(4,5-dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)phenylmethyl]phenyl-, diethyl ester (9CI) (CA INDEX NAME)



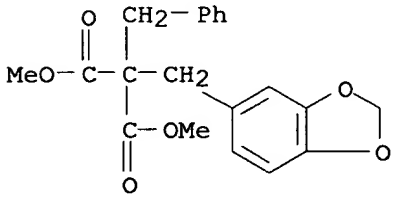
L5 ANSWER 34 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1980:471212 CAPLUS

DN 93:71212

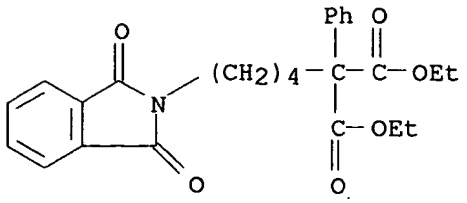
TI Dependence of aryl ether acylation upon Lewis acid stoichiometry

AU Buckley, Thomas F., III; Rapoport, Henry
CS Dep. Chem., Univ. California, Berkeley, CA, 94720, USA
SO Journal of the American Chemical Society (**1980**), 102(9), 3056-62
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
OS CASREACT 93:71212
AB Acylation of alkyl aryl ethers depends on the stoichiometry of the Friedel-Crafts catalyst. With 100 mol% catalyst, acylation proceeds rapidly and in high yield; with large molar excesses of catalyst, the reaction is essentially completely arrested. This inhibition can be reversed by using sterically bulky alkyl groups, which effectively prevent complexing between catalyst and aryl ether. Based on these observations, processes were developed for regioselective intramol. acylation of either a Ph or an alkoxylated Ph ring when both are present.
IT **74402-07-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis-decarboxylation of)
RN 74402-07-6 CAPLUS
CN Propanedioic acid, (1,3-benzodioxol-5-ylmethyl)(phenylmethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 35 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1980:460855 CAPLUS
DN 93:60855
TI Phenobarbital specific antibody production: preparation 5-phenyl-5-(4-aminobutyl) barbituric acid-bovine serum albumin conjugate
AU Castro, Albert; Chung, Alfred; Monji, Nobuo
CS Sch. Med., Univ. Miami, Miami, FL, 33101, USA
SO Research Communications in Chemical Pathology and Pharmacology (**1980**), 28(2), 309-17
CODEN: RCOCB8; ISSN: 0034-5164
DT Journal
LA English
AB The aminobutyl derivative of phenobarbital, 5-phenyl-5-(4-aminobutyl)barbituric acid hydrochlodride [42240-88-0] was synthesized through two synthetic pathways for the preparation of immunogen in production of
phenobarbital [50-06-6] specific antibody. The produced antiserum had high titer, specificity, affinity, and sensitivity (0.5 ng/mL), when examined by radioimmunoassay.
IT **74385-16-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with urea)
RN 74385-16-3 CAPLUS

CN Propanedioic acid, [4-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)butyl]phenyl-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 36 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1979:87434 CAPLUS
DN 90:87434
TI Total synthesis of (±)-picropodophyllone and (±)-4'-demethylpicropodophyllone
IN Kende, Andrew S.
PA University of Rochester, USA
SO U.S., 8 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4122092	A	19781024	US 1977-827487	19770825 <--
	CA 1088952	A1	19801104	CA 1978-309690	19780821 <--
	GB 2003152	A	19790307	GB 1978-34349	19780823 <--
	GB 2003152	B2	19820120		
	GB 2017695	A	19791010	GB 1979-10536	19780823 <--
	GB 2017695	B2	19820120		
	CH 636870	A	19830630	CH 1978-8927	19780823 <--
	DE 2837033	A1	19790322	DE 1978-2837033	19780824 <--
	DE 2837033	C2	19880421		
	JP 54095572	A2	19790728	JP 1978-102367	19780824 <--
	JP 61025033	B4	19860613		
	ES 472864	A1	19791016	ES 1978-472864	19780825 <--
PRAI	US 1977-827487	A	19770825		

GI

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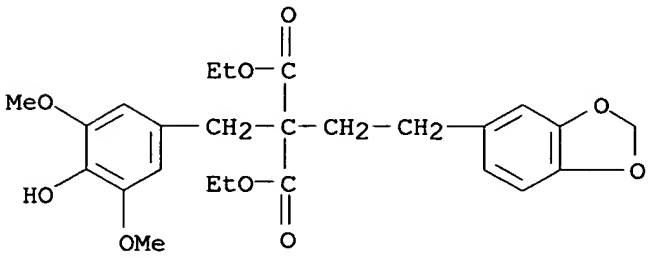
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

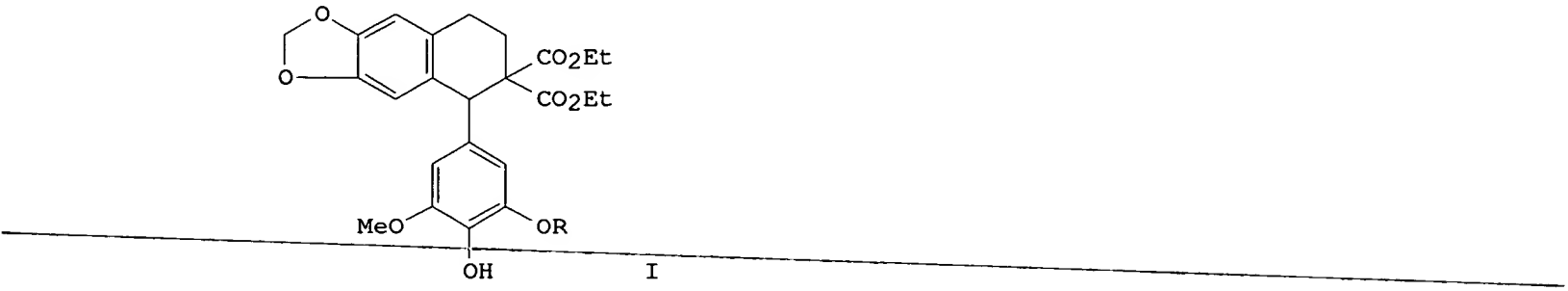
AB Methylenedioxytetralonedicarboxylates I (R = alkyl, R1 = H), intermediates in synthesis of the title compds., were prepared by cyclization of benzodioxoles II with Tl(OAc)3. Thus, II (R = Et, R1 = Me) was cyclized with Tl(OAc)3 to give I (R = Et, R1 = Me), which was oxidized followed by hydrolysis-decarboxylation and cyclization with HCHO to give (±)-3-hydroxymethylpicropodophyllone, which was treated with Jones reagent to give (±)-picropodophyllone (III).

IT **66655-29-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

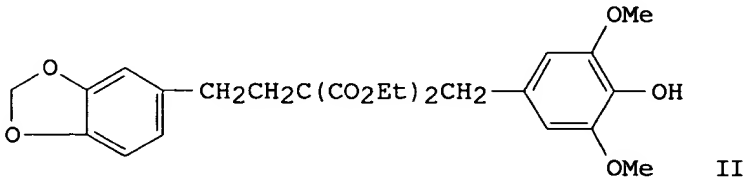
(preparation and cyclization of)
RN 66655-29-6 CAPLUS
CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(4-hydroxy-3,5-dimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 37 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1978:424198 CAPLUS
DN 89:24198
TI Product control in oxidative aryl-benzyl coupling of a phenolic 1,4-diarylbutane
AU Kende, Andrew S.; Rutledge, P. Stewart
CS Dep. Chem., Univ. Rochester, Rochester, NY, USA
SO Synthetic Communications (**1978**), 8(4), 245-50
CODEN: SYNCAV; ISSN: 0039-7911
DT Journal
LA English
GI



I



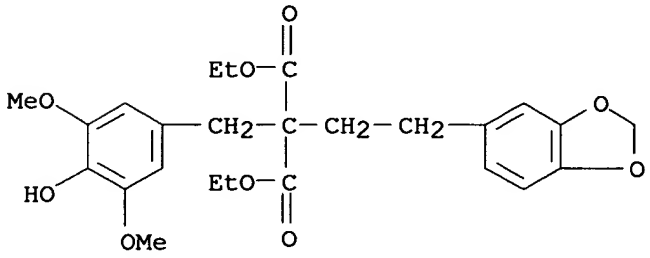
II

AB Naphthodioxole I (R = H) was prepared in 66% yield by cyclization of II in presence of Tl(O2CCF3)2. Addnl. obtained was 55% I (R = Me).
IT **66655-29-6**

RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclization of, by thallium bis(trifluoroacetate))

RN 66655-29-6 CAPLUS

CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(4-hydroxy-3,5-dimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 38 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1978:120902 CAPLUS

DN 88:120902

TI Synthetic studies on lignan lactones: aryl dithiane route to (±)-podorhizol and (±)-isopodophyllotoxone and approaches to the stegane skeleton

AU Ziegler, Frederick E.; Schwartz, John A.

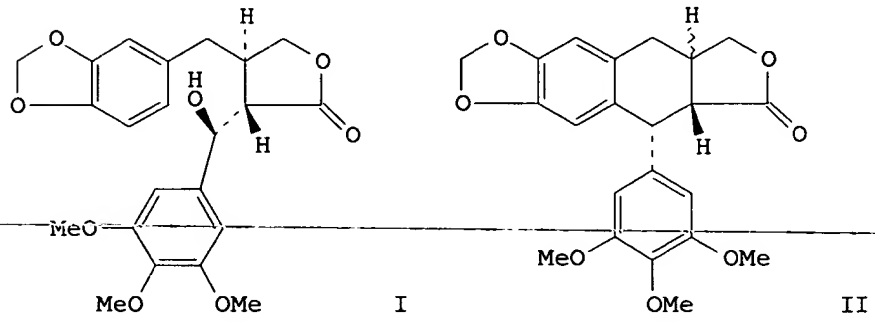
CS Sterling Chem. Lab., Yale Univ., New Haven, CT, USA

SO Journal of Organic Chemistry (**1978**), 43(5), 985-91
CODEN: JOCEAH; ISSN: 0022-3263

DT Journal

LA English

GI



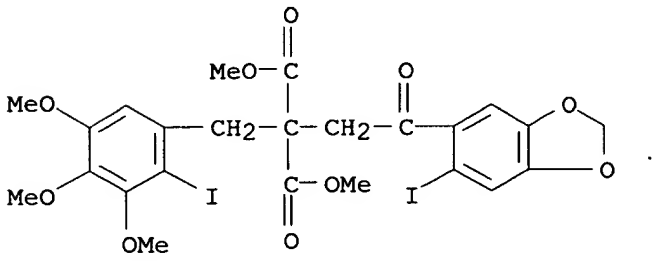
AB The conjugate addition of aryl dithiane anions to 2-butenolide was discussed. The results of the trapping of the resultant lactone enolates with an aryl halide and aryl aldehyde are detailed. The transformation of these intermediates into podorhizol (I) and isopodophyllotoxone II was also explored. The structures of products from attempted intramol. Ullmann couplings in the stegane series were established.

IT **64490-60-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation and reaction of, with cuprous complexes)

RN 64490-60-4 CAPLUS

CN Propanedioic acid, [2-(6-iodo-1,3-benzodioxol-5-yl)-2-oxoethyl][(2-iodo-3,4,5-trimethoxyphenyl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)



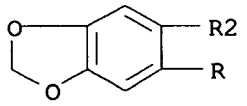
IT **64521-00-2P 64521-01-3P**

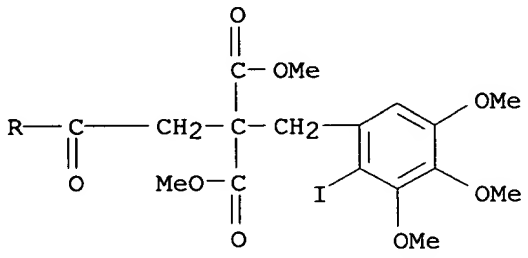
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 64521-00-2 CAPLUS

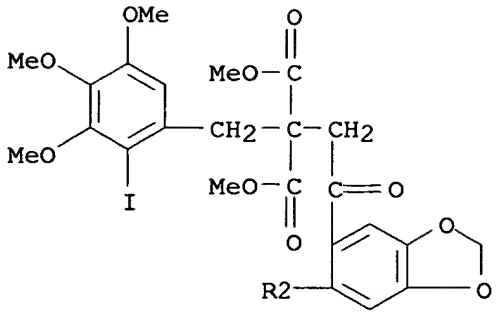
CN [5,5'-Bi-1,3-benzodioxole]-6,6'-dibutanoic acid, α,α'-bis[(2-iodo-3,4,5-trimethoxyphenyl)methyl]-α,α'-bis(methoxycarbonyl)-γ,γ'-dioxo-, dimethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

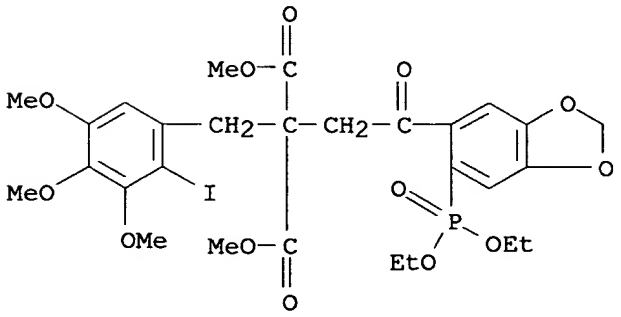




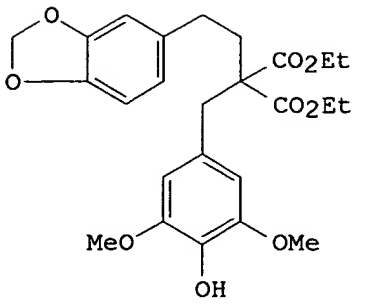
PAGE 2-A



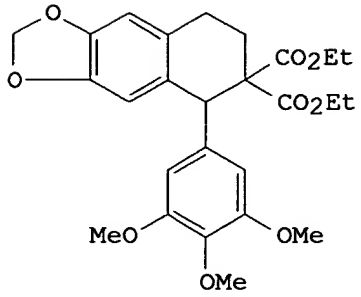
RN 64521-01-3 CAPLUS
CN Propanedioic acid, [2-[6-(diethoxyphosphinyl)-1,3-benzodioxol-5-yl]-2-oxoethyl][(2-iodo-3,4,5-trimethoxyphenyl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)



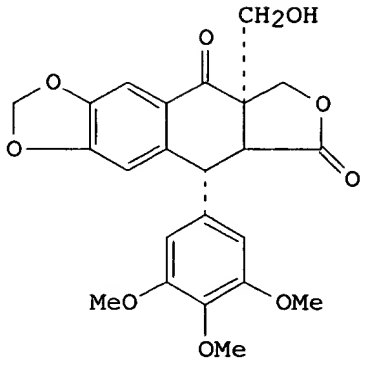
L5 ANSWER 39 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1978:6782 CAPLUS
DN 88:6782
TI Oxidative aryl-benzyl coupling. A biomimetic entry to podophyllin lignan lactones
AU Kende, Andrew S.; Liebeskind, Lanny S.; Mills, John E.; Rutledge, P. Stewart; Curran, Dennis P.
CS Dep. Chem., Univ. Rochester, Rochester, NY, USA
SO Journal of the American Chemical Society (**1977**), 99(21), 7082-3
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
GI



I



II



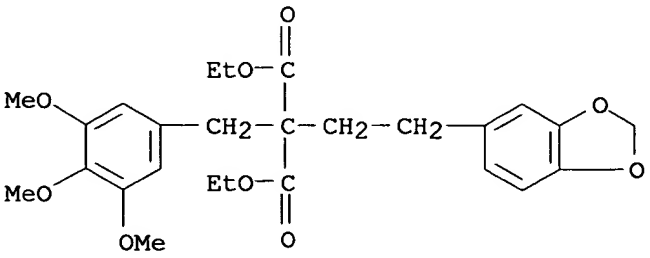
III

AB Thallium(III) trfluoroacetate oxidation of the phenolic 1,4-diarylbutane I leads to the formation of the 1-aryltetralin ring system characteristic of podophyllin lignan lactones. The tricyclic diester II obtained from I after reductive workup and methylation can be oxidized to the C-4 ketone in one step in 90% yield. Hydrolysis, decarboxylation and reaction with HCHO and base yields the hydroxylactone III, which on thermal or oxidative retroaldolization gives (±)-picropodophyllone (IV) in 13% overall yield from I. The probable role of o-quinone in the oxidative cyclization of I is discussed.

IT **58745-52-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and oxidation of)

RN 58745-52-1 CAPLUS

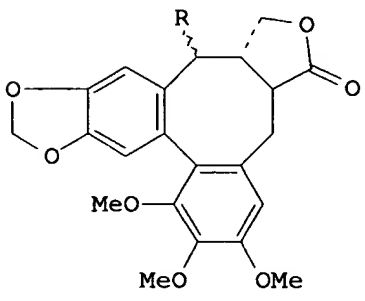
CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(3,4,5-trimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



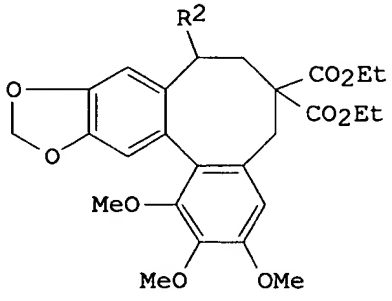
L5 ANSWER 40 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1977:189909 CAPLUS
DN 86:189909
TI Total synthesis of steganacin and derivatives
IN Kende, Andrew S.; Liebeskind, Lanny S.
PA USA
SO U.S., 22 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 4003916	A	19770118	US 1975-642954	19751222 <--
PRAI US 1975-642954	A	19751222		

GI



I

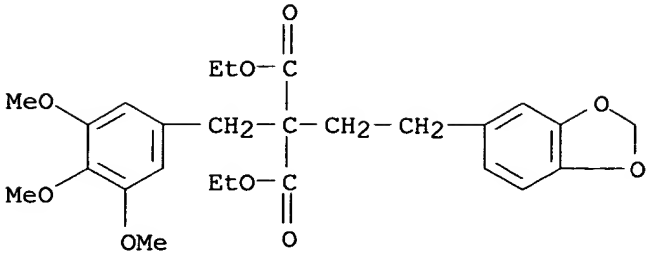


II

AB The title compds. (I, R = α-OH, β-OH, β-OAc) were prepared by mesylating homopiperonyl alc. (R1OH), treating R1O3SMe with CH(CO2Et)2, treating R1CH(CO2Et)2 with 3,4,5-(MeO)3C6H2CH2Br, cyclizing R1C(CO2Et)2CH2C6H2(OMe)3-3,4,5, oxidizing II (R2 = H) with benzoyl peroxide, oxidizing II (R2 = OH) with Jones reagent, decarboxylating the ketone, cyclizing the monoester with CH2O, and reducing with NaBH4 to give I (R = α-OH, β-OH). I (R = β-OH) was esterified to I (R = β-OAc, β-O2CCMe:CHMe).

IT **58745-52-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)

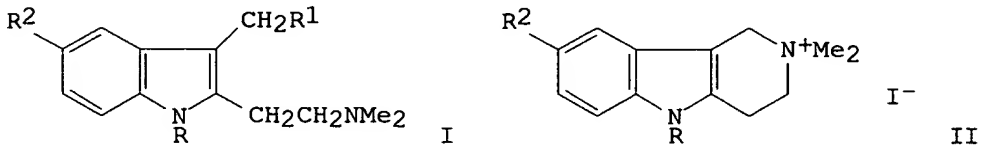
RN 58745-52-1 CAPLUS
CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(3,4,5-trimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 41 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1976:150497 CAPLUS
DN 84:150497
TI 3-Substituted isotryptamine derivatives
IN Zinnes, Harold; Schwartz, Martin L.
PA Warner-Lambert Co., USA
SO U.S., 9 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3931230	A	19760106	US 1974-460397	19740412 <--
PRAI US 1974-460397	A	19740412		

GI

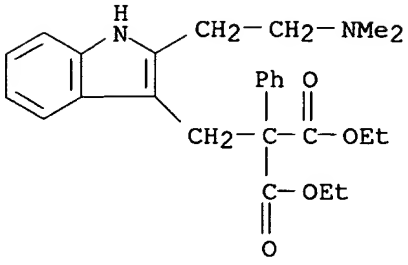


AB Eighteen isotryptamines I [R = R2 = H, R1 = cyano, 4,4-dimethyl-2,6-dioxocyclohexyl, CMe2NO2, CH(SO2Ph)2, CH(CO2Me)2, CR3(CO2Et)2 (R3 = Me, Ph, NHAc), 2-oxo-1-phenylcyclohexyl, CPh2CN, CPh2Ac, P(O)(OEt)2, CSNMe2, SO2Ph; R = Me, R1 = CMe2NO2, cyano, R2 = H; R = H, R1 = CMe(CO2Et)2, R2 = MeO, Br] or their HCl salts were prepared by reaction of γ-carbolines II with an anion (R1)-. The anion was used as the com. available Na salt (e.g., NaCN) or prepared in situ by treatment of the conjugate acid with a base. I [R = Me; R1 = cyano, CPh2CN, 2-oxo-1-phenylcyclohexyl, CMe(CO2Et)2; R2 = H] were prepared by methylation (MeI) of I (R = H, R1 and R2 as above). I (R = H, Me; R1 = CONH2, R2 = H) was prepared by aqueous hydrolysis of I (R1 = cyano), I (R = R2 = H, R1 = CO2Et.HCl) by treating I (R1 = cyano) with HCl in EtOH, and I (R = Me, R1 = CPh2H, R2 = H) and its HCl salt by refluxing I (R1 = CPh2CN, R and R2 as above) with MeLi 20 hr in C6H6. I are useful as sedatives and antiagression agents (no data).

IT **58981-74-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 58981-74-1 CAPLUS
CN Propanedioic acid, [[2-[2-(dimethylamino)ethyl]-1H-indol-3-

yl]methyl]phenyl-, diethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

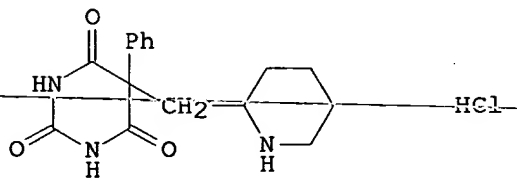


● HCl

L5 ANSWER 42 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1976:140749 CAPLUS
DN 84:140749
TI Antiparkinsonism compositions
IN Wiggins, Leslie F.; James, John William; Gittos, Maurice W.
PA Aspro-Nicholas Ltd., UK
SO U.S., 16 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3930006	A	19751230	US 1965-510108	19650722 <--
	US 3857844	A	19741231	US 1966-526707	19660211 <--
PRAI	US 1960-75911	A2	19601215		
	US 1963-276977	A3	19630430		
	US 1963-277431	A2	19630502		

GI



I

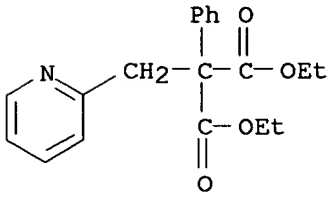
AB Barbituric and thiobarbituric acid derivs. useful for ameliorating symptoms of paralysis agitans associated with Parkinsonism are reported. 5-Phenyl-5-(2-piperidinylmethyl)barbituric acid-HCl (I) [20432-72-8], the preferred compound of the invention, compared favorably with atropine, kemadrine, and aturbán in controlling paralysis agitans while being less toxic and avoiding atropine-like side effects. Syntheses and pharmaceutical formulations are reported. E.g. di-Et 2-(2-pyridylmethyl)-2-phenylmalonate [**3310-07-4**] was added to Na and thiourea [62-56-6] and worked up to give 5-(2-pyridylmethyl)-5-phenyl-2-

thiobarbituric acid [1454-06-4] which was oxidized using HNO3 to 5-(2-pyridylmethyl)-5-phenylbarbituric acid [1454-05-3] which was reduced under acidic conditions to give I. Tablets each containing I 100, lactose 228, maize starch 70, Et cellulose 8, talc 20, and stearic acid 4 mg were prepared

IT **3310-07-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

RN 3310-07-4 CAPLUS

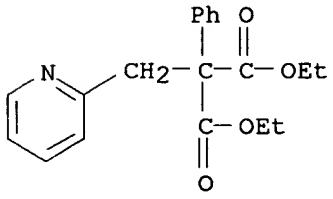
CN Propanedioic acid, phenyl(2-pyridinylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



IT **1454-12-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 1454-12-2 CAPLUS

CN Propanedioic acid, phenyl(2-pyridinylmethyl)-, diethyl ester, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L5 ANSWER 43 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1976:90045 CAPLUS

DN 84:90045

TI Total synthesis of (+-)-steganacin

AU Kende, Andrew S.; Liebeskind, Lanny S.

CS Dep. Chem., Univ. Rochester, Rochester, NY, USA

SO Journal of the American Chemical Society (**1976**), 98(1), 267-8
CODEN: JACSAT; ISSN: 0002-7863

DT Journal

LA English

OS CASREACT 84:90045

GI For diagram(s), see printed CA Issue.

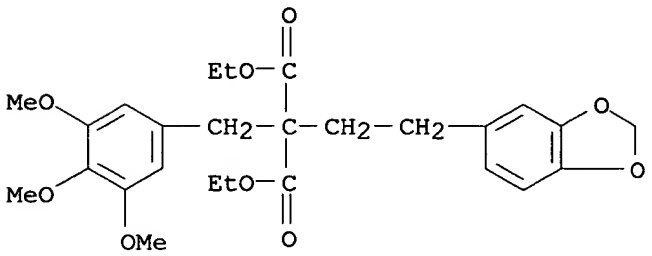
AB The total synthesis of the antileukemic dibenzocyclooctadiene lignan

lactone steganacin (I, R = COMe) in the racemic form, along with companion lactones (±)-steganol (I, R = H) and (±)-steganone (II), was achieved starting from homopiperonyl alc. Formation of the 8-membered ring was carried out by VOF3 nonphenolic oxidative coupling, and C-5 O was regiospecifically introduced using N-bromosuccinimide, followed by silver trifluoroacetate. The yield from homopiperonyl alc. to (±)-steganone was 10% over 8 steps.

IT **58745-52-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)

RN 58745-52-1 CAPLUS

CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(3,4,5-trimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 44 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1974:70639 CAPLUS

DN 80:70639

TI Indole derivatives. LXXXVII. Improvement in the synthesis of skatyl- and substituted skatylmalonic esters

AU Suvorov, N. N.; Velezheva, V. S.; Vampilova, V. V.

CS Mosk. Khim.- Tekhnol. Inst. im. Mendeleeva, Moscow, USSR

SO Khimiya Geterotsiklicheskikh Soedinenii (**1973**), (11), 1512-14
CODEN: KGSSAQ; ISSN: 0132-6244

DT Journal

LA Russian

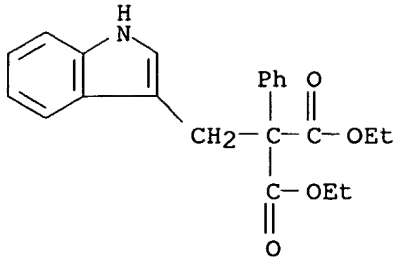
GI For diagram(s), see printed CA Issue.

AB Gramine methiodide condensed with CHR(CO2Et)2 Na salt (R = H, Et, Bu, Ph) in DMF at .apprx.100° in a N atmospheric to give the corresponding skatylmalonates I in 90-5% yield.

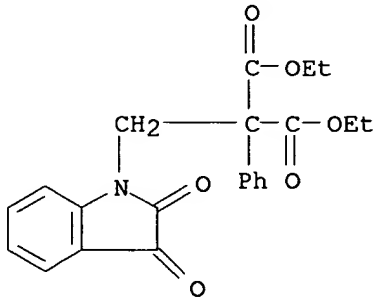
IT **51843-46-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 51843-46-0 CAPLUS

CN Propanedioic acid, (1H-indol-3-ylmethyl)phenyl-, diethyl ester (9CI) (CA INDEX NAME)



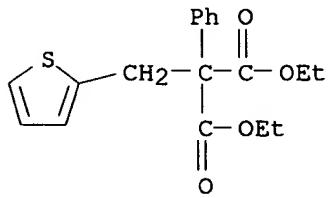
L5 ANSWER 45 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1974:14805 CAPLUS
DN 80:14805
TI N-(α-Haloalkyl)carboxamides. 19. Reactions of N-(chloromethyl)isatin with prototropically active compounds
AU Boehme, H.; Schwartz, H.
CS Pharm.-Chem. Inst., Univ. Marburg, Marburg/L., Fed. Rep. Ger.
SO Archiv der Pharmazie (Weinheim, Germany) (**1973**), 306(9), 684-92
CODEN: ARPMAS; ISSN: 0365-6233
DT Journal
LA German
GI For diagram(s), see printed CA Issue.
AB Reaction of N-(chloromethyl)isatin (I) with RCH(CO2Et)2 or Ph2CHCHO gave the isatins II (R = Me or Ph) and III, resp. Reaction of I with HNRR1 gave the isatins IV (R = R1 = Et, NRR1 = piperidino or morpholino). Reaction of I with alkoxides, phenoxides, and carboxylates gave the ethers and esters V [R = Me, Et, CMe3, Pr, C6H3(NO2)2-2,4, or COPh]. Reaction of I with thiols gave the sulfides VI [R = Me, Et, CH2CH2OH, CH2CO2H, CH2CO2Et, 2,5-Cl2C6H3, or 2,4-(O2N)2C6H3]. Reaction of I with alkali metal dithiocarbamates gave the dithiocarbamates VII (R = Me, Et, Ph, or CH2Ph; R1 = H, Me, Et, or Ph; NRR1 = 1-pyrrolidinyl, piperidino, morpholino, or hexahydro-1-azepinyl).
IT **50899-37-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 50899-37-1 CAPLUS
CN Propanedioic acid, [(2,3-dihydro-2,3-dioxo-1H-indol-1-yl)methyl]phenyl-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 46 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1974:3401 CAPLUS
DN 80:3401
TI Pharmaceutical (hexamethylenimino)alkyl compounds
IN Robba, Max F.; Duval, Denise J. C.
PA Innothera
SO Ger. Offen., 38 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

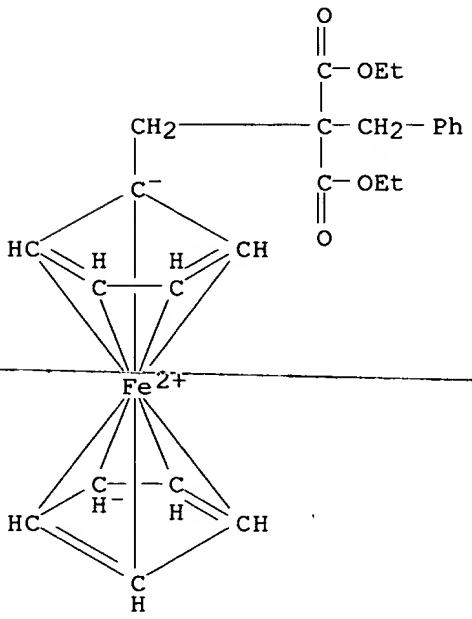
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2313338	A1	19731004	DE 1973-2313338	19730317 <--
	DE 2313338	B2	19800626		
	DE 2313338	C3	19810409		
	FR 2176473	A1	19731102	FR 1972-9639	19720320 <--
	FR 2219776	A1	19740927	FR 1973-7505	19730302 <--
	GB 1392671	A	19750430	GB 1973-13910	19730322 <--
	CA 1003831	A1	19770118	CA 1973-167040	19730326 <--
	JP 48099190	A2	19731215	JP 1973-37370	19730330 <--
	JP 51011117	B4	19760408		
PRAI	FR 1972-9639	A	19720320		
	FR 1973-7505	A	19730302		

GI For diagram(s), see printed CA Issue.
AB About 60 esters or amides (I, n = 2 or 3; X = O or NH; R = e.g. cyclohexyl, Ph, C6H4Cl-p, C6H4Br-p, CH2Ph, R1 = R, C1-5 alkyl, 2- or 3-thienyl, 2-thenyl, furfuryl, or 2-benzothienyl), β-(hexamethylenimino)ethyl (+)-cyclohexyl(3-thienyl)acetate, and their hydrochlorides, citrates, or oxalates were prepared and used as analgesics, vasodilators, local anesthetics, and spasmolytics. Thus, 4-BrC6H4CH(C6H4Cl-4)CO2H and β-(hexamethylenimino)ethyl chloride was refluxed in Me2-CHOH for 17 hr to give, after treatment with (CO2H)2, 70% I oxalate (n = 2, X = O, R = C6H4Br-4, R1 = C6H4Cl-4). DL-Et cyclohexyl(3-thienyl)acetate and β-hexamethylenimino)ethanol was heated in PhMe in the presence of Na to give 70% DL-I (n = 2, X = O, R = cyclohexyl, R1 = 3-thienyl), which was resolved into the D and L form via the quinine salts. Ph2CH-COCl and [2-(hexamethylenimino)ethyl]amine was refluxed in C6H6 to give 50% I.HCl (n = 2, X = NH, R = R1 = Ph).
IT **51535-44-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 51535-44-5 CAPLUS
CN Propanedioic acid, phenyl(2-thienylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 47 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1972:59727 CAPLUS
DN 76:59727
TI Metallocenes. XVIII. Stereochemistry of heterobridged and homobridged ferrocene ketones and alcohols
AU Gautheron, Bernard; Leblanc, Jean C.
CS Fac. Sci. Fondam. Appl., Univ. Dijon, Dijon, Fr.
SO Bulletin de la Societe Chimique de France (**1971**), (10), 3629-36
CODEN: BSCFAS; ISSN: 0037-8968
DT Journal
LA French
GI For diagram(s), see printed CA Issue.
AB Dimethylaminomethylferrocene methyl iodide in HCONMe2 was condensed with RCH(CO2Et)2 in the presence of Na in PhMe; hydrolysis and decarboxylation of the products gave substituted ferrocenylpropionic acids. Cyclization of the acids with (CF3CO)2O, polyphosphoric acid, or by intramol. Friedel-Crafts reactions gave essentially heteroannular bridged ketones (I) and small amts. of homoannular bridged ketones (II, R=Me2CH, PhCH2, Bu, Et). I and II were isolated in racemic and active series and their reduction was stereospecific. Anal. of I by NMR and CD for active compds. suggested a specific conformation which agreed with the observed asym. induction and the "kinetic resolution" of the optically active carbinols (III).
IT **36655-55-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 36655-55-7 CAPLUS
CN Ferrocene, 1-[2,2-bis(ethoxycarbonyl)-3-phenylpropyl]- (9CI) (CA INDEX NAME)



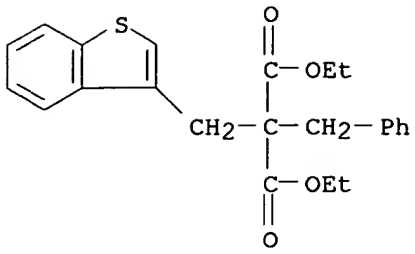
L5 ANSWER 48 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1972:59436 CAPLUS
DN 76:59436

TI Spasmolytic-vasodilating β-(3-benzo[b]thienyl)propionic acid derivatives
IN Robba, Max F.; Duval, Denise J. C.
PA Innothera
SO Ger. Offen., 39 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

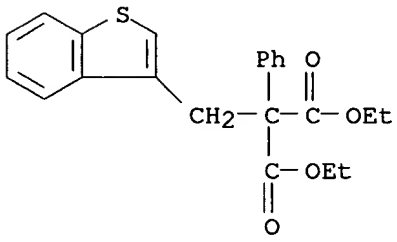
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2128887	A	19711216	DE 1971-2128887	19710611 <--
	DE 2128887	B2	19730913		
	DE 2128887	C3	19740418		
	FR 2092731	A5	19720128	FR 1970-21679	19700612 <--
	FR 2092731	B1	19730810		
	US 3865842	A	19750211	US 1971-150747	19710607 <--
	GB 1318473	A	19730531	GB 1971-27563	19710611 <--
	JP 50028434	B4	19750916	JP 1971-42068	19710612 <--
	US 3954780	A	19760504	US 1974-489545	19740718 <--
	US 4035371	A	19770712	US 1976-651223	19760122 <--
PRAI	FR 1970-21679	A	19700612		
	US 1971-150747	A3	19710607		
	US 1974-489545	A3	19740718		

GI For diagram(s), see printed CA Issue.
AB The title compds. (I; R=e.g. CH2CH:CH2, PhCH2, or 2-thenyl; R1=e.g. H, CH2CH2NEt2, β-pyrrolidinoethyl, β-morpholinoethyl, or 1-piperidino-2-propyl) of LD50 .apprx.100-320 mg/kg i.p. in mice, the spasmolytic, vasodilating, antiserotonin, and local anesthetic activities of which were tested in rats and guinea pigs, were prepared by condensation of 3-(chloromethyl)benzo[b]thiophene (II) with RCH(CO2Et)2 in the presence of NaOEt, hydrolysis, saponification, decarboxylation via the free acids followed by aminoalkylation. Thus, CH2:CHCH2CH(CO2Et)2 was refluxed 1 hr with Na in EtOH, II in EtOH added, and the mixture refluxed 17 hr to give 70% Et allyl(benzo[b]thien-3-ylmethyl)malonate, which on 15 hr reflux with KOH-PhCH2OH gave 80% I (R=CH2:CHCH2, R1=H). Five other malonates and corresponding I (R1=H) were similarly prepared I (R=Ph, R1=H) and ClCH2CH2NEt2 in iso-PrOH was refluxed 17 hr to give I (R=Ph, R1=CH2CH2NEt2), which was isolated as crystalline oxalate in 65% yield. Similarly prepared were 55 other I salts.
IT **35062-44-3P 35062-45-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 35062-44-3 CAPLUS
CN Propanedioic acid, (benzo[b]thien-3-ylmethyl)(phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



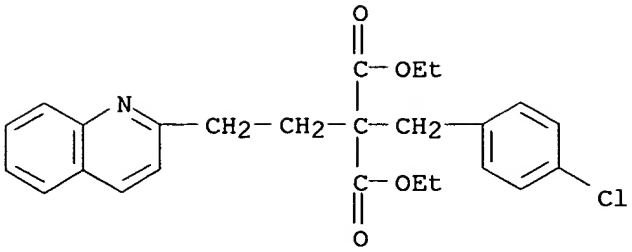
RN 35062-45-4 CAPLUS
CN Propanedioic acid, (benzo[b]thien-3-ylmethyl)phenyl-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 49 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1971:12977 CAPLUS
DN 74:12977
TI Synthesis of quinolizine derivatives. XXIII. Synthesis of perhydrobenzo[c]quinolizine and benzo[c]quinolizidine derivatives
AU Akiba, Mitsuo; Ohki, Sadao
CS Tokyo Coll. Pharm., Tokyo, Japan
SO Yakugaku Zasshi (**1970**), 90(10), 1193-200
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Japanese
GI For diagram(s), see printed CA Issue.
AB Perhydrobenzo[c]quinolizine derivs. I and II and a benzo[c]quinolizidine derivative (III) were synthesized from quinaldine involving di-Et β-(2-quinoyl)ethylmalonate intermediates.
IT 30015-42-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 30015-42-0 CAPLUS
CN Malonic acid, (p-chlorobenzyl)[2-(2-quinolyl)ethyl]-, diethyl ester, monopicrate (8CI) (CA INDEX NAME)

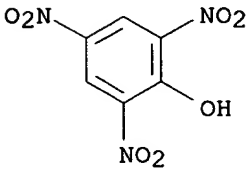
CM 1

CRN 47674-45-3
CMF C25 H26 Cl N O4



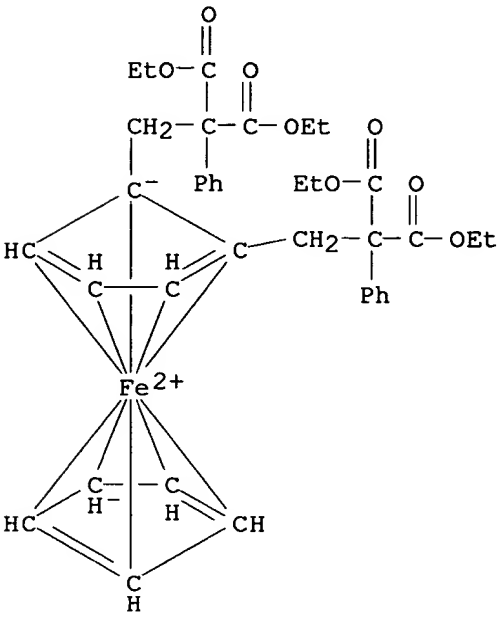
CM 2

CRN 88-89-1
CMF C6 H3 N3 O7



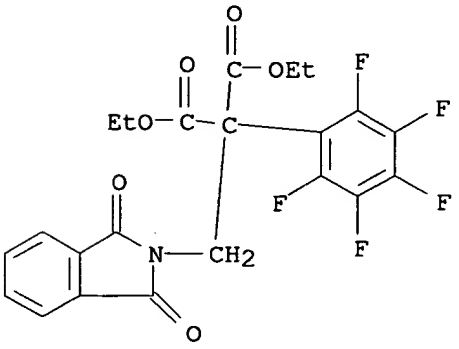
L5 ANSWER 50 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1970:520733 CAPLUS
DN 73:120733
TI Metallocenes. XV. Application of a specific reaction of ferrocenylcarbinols to the synthesis of mono and 1,2-disubstituted ferrocenes. Study of several stereochemical problems
AU Moise, Claude; Tirouflet, Jean
CS Lab. Chim. Org. Gen., Fac. Sci., Dijon, Fr.
SO Bulletin de la Societe Chimique de France (**1970**), (7), 2656-65
CODEN: BSCFAS; ISSN: 0037-8968
DT Journal
LA French
GI For diagram(s), see printed CA Issue.
AB 1,2-HOCH2FcCH2N+Me3 I- (I, FcH2 = ferrocene) reacted with refluxing alc. NaCR(CO2Et)2 (II, R = H, Me, Ph) to give the corresponding 1,2-Fc[CH2Cr(CO2Et)2]2, which gave 1,2-Fc(CH2CHRCO2H)2 (III) after saponification and heating to 180° with powdered Cu. Treatment of III (R = H) with (CF3CO)2O in CH2Cl2 afforded IV, which was reduced to V by Zn(Hg) and HCl. Reaction of V with (CF3CO)2O in CH2Cl2 gave a mixture of VI and VII. KBH4 reduction of VI gave a racemic mixture of alcs. LiAlH4 reduction of VII gave only the endo-alc., which was converted to the exo isomer by refluxing the endo-acetate in aqueous Me2CO 40 hr. The Et ester of IV was reduced to VIII by NaBH4. HFcCH2OH likewise reacted with II, and HFcCR1R2OH (R1, R2 = H, Me, Ph) reacted with II (R = H) to form HFcCR1R2CH(CO2Et)2; the latter was decarboxylated to give HFcCR1R2CH2CO2H (IX). IX (R1, R2 = Me) was cyclized and reduced with KBH4 as above. These reactions were possible due to the stability of HFcCR1R2+. The stereochemistry of the reactions is discussed.

IT **31852-27-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 31852-27-4 CAPLUS
CN Malonic acid, (1,2-ferrocenediyldimethylene)bis[phenyl-, tetraethyl ester (8CI) (CA INDEX NAME)

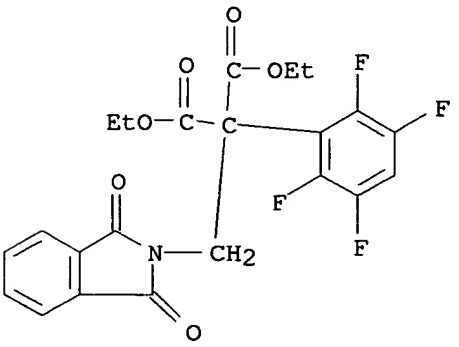


L5 ANSWER 51 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1970:413946 CAPLUS
DN 73:13946
TI Aromatic fluoro derivatives. XL. Effect of a pentafluorophenyl ring on the strength of CH-acids
AU Vlasov, V. M.; Krivousova, E. D.; Yakobson, G. G.
CS Novosibirsk. Inst. Org. Khim., Novosibirsk, USSR
SO Zhurnal Organicheskoi Khimii (**1970**), 6(4), 758-67
CODEN: ZORKAE; ISSN: 0514-7492
DT Journal
LA Russian
AB The action of NaH on C6F5CH2CN in MeOCH2CH2OMe (I) solution gives p-NCCH2C6F4CH(CN)C6F5 (II) which at -10° to 25° forms with the excess NaH colored carbanion p-NCCH2C6F4C-(Na+)(CN)C6F5 (III). The existence of III was established by ir and NMR spectroscopy. The hydrolysis of II gave the corresponding dicarboxylic acid. Similarly, C6F5CH(CO2Et)2 in I solution gave stable C6F5C-(Na+)(CO2Et)2 (IV). The comparison of IV NMR spectra in I and PO(NMe2)3 (highly polar solvent) with the spectra of RC-(Na+)(CO2Et)2 (V) [R is p-HC6F4, 2,4-(O2N)2C6H3, o-O2NC6H4, p-O2HC6H4, or Ph] shows that the ionization of IV is of the same order as that of V (R = o-O2NC6H4 or p-O2NC6H4). The position of equilibrium was established in RCH(CO2Et)2 + IV .dblharw. V + C6F5CH(CO2Et)2 systems. The relative reactivity of IV and V toward N-chloromethylphthalimide was determined
IT **28744-78-7P 28744-79-8P 28744-80-1P**

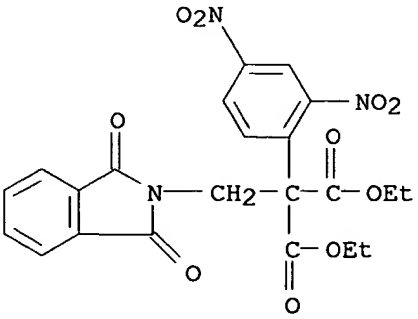
28744-81-2P 28744-82-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 28744-78-7 CAPLUS
CN Malonic acid, (pentafluorophenyl)(phthalimidomethyl)-, diethyl ester (8CI)
(CA INDEX NAME)



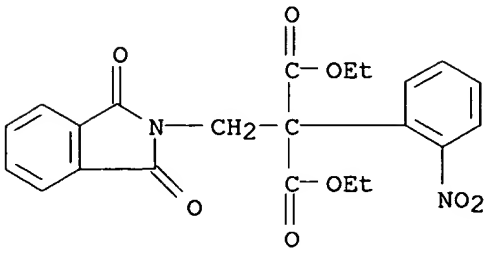
RN 28744-79-8 CAPLUS
CN Malonic acid, (phthalimidomethyl)(2,3,5,6-tetrafluorophenyl)-, diethyl ester (8CI) (CA INDEX NAME)



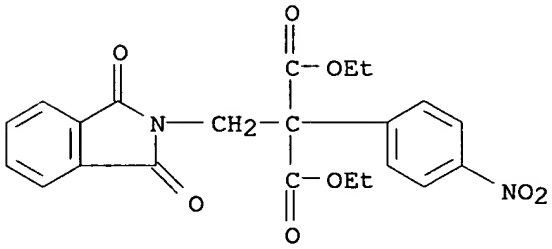
RN 28744-80-1 CAPLUS
CN Malonic acid, (2,4-dinitrophenyl)(phthalimidomethyl)-, diethyl ester (8CI)
(CA INDEX NAME)



RN 28744-81-2 CAPLUS
CN Malonic acid, (o-nitrophenyl)(phthalimidomethyl)-, diethyl ester (8CI) (CA INDEX NAME)

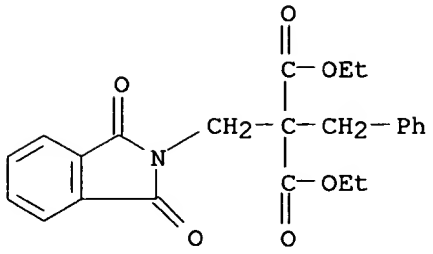


RN 28744-82-3 CAPLUS
CN Malonic acid, (p-nitrophenyl)(phthalimidomethyl)-, diethyl ester (8CI) (CA INDEX NAME)

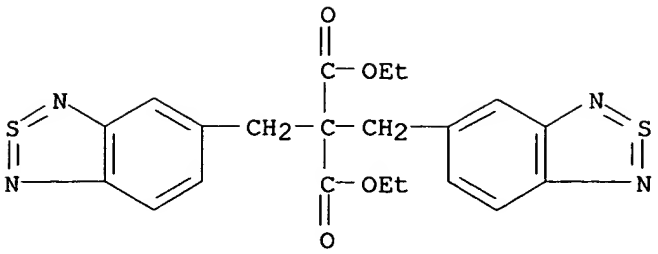


L5 ANSWER 52 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1970:101087 CAPLUS
DN 72:101087
TI Analogs of angiotensin II. I. Solid phase synthesis
AU Chaturvedi, N. C.; Park, Won Kil; Smeby, R. R.; Bumpus, F. M.
CS Res. Div., Cleveland Clin. Found., Cleveland, OH, USA
SO Journal of Medicinal Chemistry (**1970**), 13(2), 177-81
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
AB [5-Ile,8-Tyr]-, [5-Ile,8-(OMe)Tyr]-, [5-Val,8-(OMe)Tyr]-, [4-(OMe)-Tyr,5-Ile]-, [4-(OMe)Tyr,5-Val]-, [1-Asp(NH2),4-(OMe)Tyr,5-Val]-, [5-Ile,7-pipecolic acid]-, [5-Ile,8-(3-amino-4-phenyl)-butyric acid]-, and [5-Ile,8-(3-amino-3'-phenyl)isobutyric acid]-angiotensins II were synthesized by the solid phase method in yields of 50-63%. All peptides were homogeneous. Insertion of OH or OMe on the Ph ring in position 8 of angiotensin II reduced pressor activity slightly. However, OMe in place of the OH of tyrosine in position 4 of angiotensin II caused a drastic reduction of pressor activity. Substitution of an unnatural amino acid in positions 7 or 8 of angiotensin II greatly reduced pressor activity.
IT **26217-38-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 26217-38-9 CAPLUS

CN Malonic acid, benzyl(phthalimidomethyl)-, diethyl ester (8CI) (CA INDEX NAME)



L5 ANSWER 53 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1970:31707 CAPLUS
DN 72:31707
TI 2,1,3-Thia- and selenadiazoles. LIX. Carboxy-, carboxymethyl-, and carboxyethylbenzo-2,1,3-thiadiazoles
AU Pesin, V. G.; D'yachenko, S. A.; Golubeva, E. V.
CS Leningrad. Khim.-Farm. Inst., Leningrad, USSR
SO Khimiya Geterotsiklicheskikh Soedinenii (**1969**), (4), 619-22
CODEN: KGSSAQ; ISSN: 0132-6244
DT Journal
LA Russian
GI For diagram(s), see printed CA Issue.
AB To a solution of 0.23 g Na in 15 ml anhydrous EtOH was added 1.6 g di-Et malonate, the mixture stirred 1 hr, and 2.29 g I (R = Br) in 25 ml dry C6H6 added, and the whole kept 10 hr to yield 81% I (R = CH2CO2H), m. 103-4° (H2O). To a solution of 0.92 g Na in 40 ml EtOH was added 6.4 g di-Et malonate, the mixture stirred 1 hr, and 9.2 g II (R = Br) in 80 ml dry EtOH added to yield 29% III (R = R1 = CO2Et) (IV), m. 105-6° (EtOH), and, from the mother liquor (after 8-10 hr reflux with 120 ml 20% HCl) 4.8 g II (R = CH2CO2H), m. 117-18° (H2O). IV (2 g) in 40 ml 10% KOH was refluxed 3 hr to give 90% III (R = H, R1 = CO2H), m. 141-2° (EtOH). To 10 ml HNO3 (d. 1.5) was added dropwise with stirring 1 g II (R = CO2H) and the mixture kept 30 min at 20° to give 73% V (R = CO2H), m . 180-2° (EtOH). To a solution of 1.5 g KCN in 75 ml EtOH and 5 ml H2O was added portionwise 2 g I (R = Br) and the whole refluxed 3 hr to yield 0.6 g VII (R = CN) (VIII), m. 192-3° (AcOH), and 1 g I (R = CN), m. 92 -3° (EtOH). VIII (1 g) in 25 ml 50% H2SO4 and 25 ml AcOH was refluxed 3 hr to yield 95% VII (R = CO2H), m. 179-80° (EtOH). To 12 ml HNO3 (d 1.5) was added portionwise at 0° during 30 min 1 g II (R = CH2CO2H), and the mixture stirred 30 min and poured on ice to yield 85% V (R = CH2CO2H), m. 153-4° (aqueous EtOH). To 15 ml HNO3 (d. 1.5) was added portionwise at 0° with stirring 1.5 g. I (R = CH2CO2H) to yield 75% VI (R = CH2CO2H), m. 137-8° (EtOH). The pK values of the acids obtained were measured and compared with those of the corresponding aromatic carboxylic acids.
IT **24786-03-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 24786-03-6 CAPLUS
CN Malonic acid, bis(2,1,3-benzothiadiazol-5-ylmethyl)-, diethyl ester (8CI) (CA INDEX NAME)



L5 ANSWER 54 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1970:21590 CAPLUS
DN 72:21590
TI β-(1-Naphthyl)propionic acid derivatives
AU Mndzhoyan, A. L.; Badalyan, V. E.
CS Inst. Tonkoi Org. Khim., Erevan, USSR
SO Armyanskii Khimicheskii Zhurnal (**1969**), 22(8), 671-87
CODEN: AYKZAN; ISSN: 0515-9628
DT Journal
LA Russian
GI For diagram(s), see printed CA Issue.
AB For the investigation of spasmolytic properties a series of amino esters of α-substituted β-(1-naphthyl)propionic acids were synthesized. By known methods were prepared the following substituted furfuryl alcs. (Ia) (R1, R2, % yield, and b.p./mm. given): H, p-MeOC6H4CH2, 84.5, 187-8°/5; H, 3,4-(MeO)2C6H3CH2, 52.7, 210-12°/5; Me, Me, 89.9, 95-6°/10; PhCH2, Me, 74.2, 167-9°/5. Mono-substituted malonic acid esters were prepared in the usual way based on chlorides. The following RCH2CH(CO2Et)2 were obtained (R, % yield, and b.p./mm. given): 2-benzofuryl (A), 67.8, 179-82°/3; 5-methyl-2-furyl (B), 37.7, 132-5°/3; 5-benzyl-2-furyl (C), 55.6, 201-3°/3; 5-(p-methoxybenzyl)-2-furyl (D), 54.7, 222-4°/1; 5-(3,4-dimethoxybenzyl)-furyl (E), 44.1, 236-8°/1; 4,5-dimethyl-2-furyl (F), 30.8, 152-4°/3; 5-methyl-4-benzyl-2-furyl (G), 58.9, 204-6°; The introduction of the second radical, α-methylnaphthyl, was described. To 0.2 mole NaOEt in 150 ml EtOH was added 0.2 mole of the resp. monosubstituted malonate, the mixture refluxed 3 hr, cooled, and treated with 0.21 mole α-(chloromethyl)naphthalene, refluxed 12 hr., poured into H2O and extracted with Et2O. The following C10H7CH2C(RCH2)(CO2Et)2 were prepared (R, % yield, and b.p./mm. given): A, 83, 254-6°/1; B, 77.5, 222-5°/1; C, 74.6, 282-4°/1; D, 74.8, 302-3°/ 0.8; E, 64.9, 307-9°/0.6; F, 55.3, 233-5°/1; G, 63.5, 297-9°/1; By sap on. and decarboxylation, the following C10H7CH2CH(RCH2)CO2H were prepared (R, % yield, b.p./mm., and m.p. given): tetrahydrofuryl (H), 82.6, 225-6°/3, -; furyl (J), 79.3, 218-20°/3, 72-4°; A, 71.5, 259-61°, 111-12°; B, 73.0, 228-30°/3, 68-70°; C, 75.2, 280-3°/1, 70-2°; D, 82.5, 274-6°/0.4, -; E, 74.2, 285-8°/0.4, 61-2°; F, 55.4, 230-2°, -; G, 70.5, 264-6°/0.4, 51-2°. The substituted acid chlorides were prepared by refluxing 0.1 mole acid in 150 ml C6H6 with 0.13 mole SOCl2 4 hr, removing the solvent and distillation in vacuo. The following α-C10H7CH2CH(CH2R)COCl were obtained (R, % yie ld, and b.p./mm given): H, 74.2, 201-2°/1; J, 78.2, 190-2°/1; A, 80.6, 228-30°/1; B, 70.5,

202-4°/1; C, 87.3, 277-80°/1; D, 75.0, 280-2/0.6; E, 69.4, 285-6°/0.4; F, 72.6, 210-2°/1; G, 74.1, 253-5°/0.6. Amino esters were prepared by refluxing 0.1 mole of the acid chloride in 100 ml C6H6 and 0.12 mole 1,2-dimethyl-3-(dimethylamino)-propanol in 30 ml C6H6 4 hr. The following amino esters α-C10H7CH2CHRCO2(CHMe)2CH2NMe 2 were prepared (R, % yield, and b.p./mm given): H, 90.6, 182-3°/1; tetra hydrofurfuryl, 46.3, 233-5°/1: furfuryl, 84.7, 226-7°/1; benzofurfuryl, 88.3, 261-62°/1; 2-methyl-5-furfuryl (K), 82.5, 233-4°/1; 2-benzyl-5-furfuryl (L), 76.3, 280-2°/0.8; 2-(p-methoxybenzyl)furfuryl (M), 77.3, 304-5°/0.6; 2-(4,5-methoxybenzyl)-5-furfuryl (N), 74.1, 302-4°/0.6; 2,3-methyl-5-furfuryl (O), 70.8, 239-40°/1; 2-methyl-3-benzyl-5-furfuryl (P), 76.3, 248-50°/0.2. The diethylamino esters were obtained similarly using HNEt2 (R, % yield, and b.p./mm. given). H, 89.8, 188-90°/1; tetrahydrofurfuryl, 42.7, 240-1°/1; furfuryl, 81.3, 233-4°/1; benzofurfuryl, 85.1, 270-1°/1; K, 83.1, 240-1°/1; L, 79.5, 2 87-8°; M, 78.8, 310-1°/0.6; N, 76.8, 308-10°/0.4; O, 72.7, 240-2°/0.8. P, 68.3, 255-6°/0.2. Some derivs. of furfuryl alc. were prepared by reduction of substituted furyl-2-carboxylates with LiAlH4.

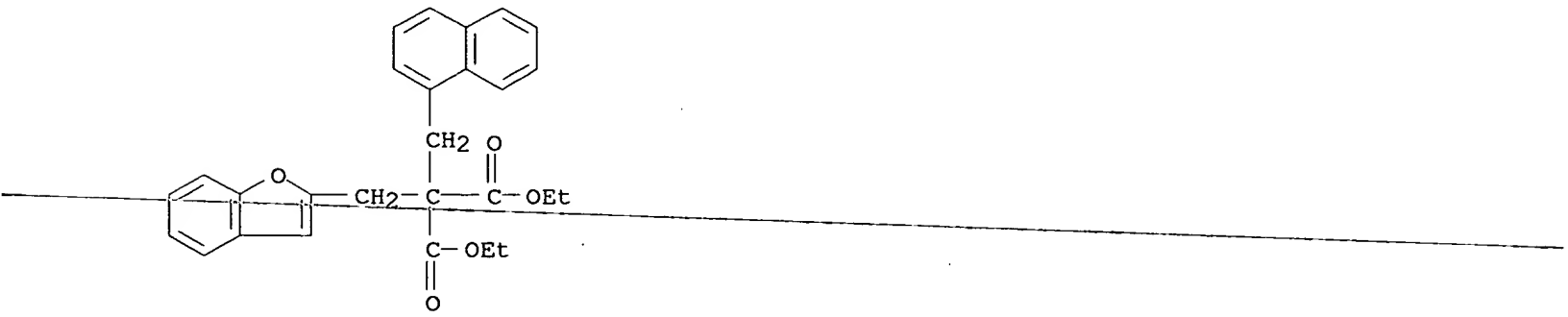
Di-Et 5-Benzylfurfurylidenemalonate, bl 220-2°, m. 43-4°, was obtained in the same way as the ester of furfurylidenemaleate. Also 95.2% 5-benzylfurfurylidenemalonic acid, m. 167° (decomposition), was prepared by saponification of the ester.

IT **25379-07-1P 25379-08-2P 25379-09-3P 25379-10-6P 25379-11-7P 25379-24-2P 25379-25-3P**

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

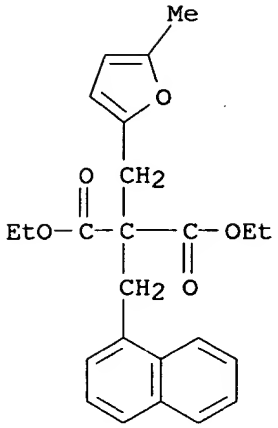
RN 25379-07-1 CAPLUS

CN Malonic acid, (2-benzofuranylmethyl)(1-naphthylmethyl)-, diethyl ester (8CI) (CA INDEX NAME)

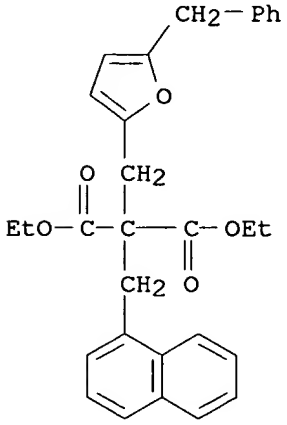


RN 25379-08-2 CAPLUS

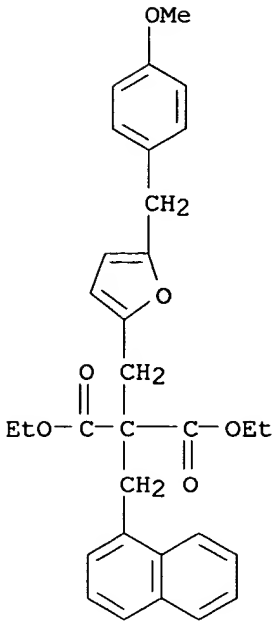
CN Malonic acid, (5-methylfurfuryl)(1-naphthylmethyl)-, diethyl ester (8CI) (CA INDEX NAME)



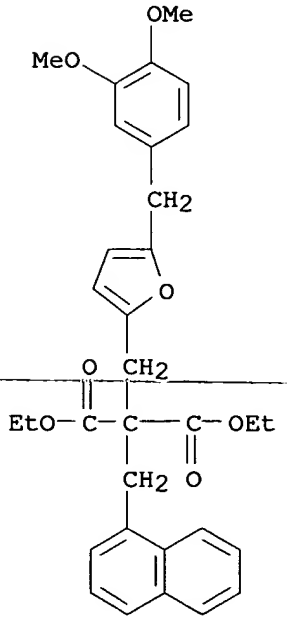
RN 25379-09-3 CAPLUS
CN Malonic acid, (5-benzylfurfuryl)(1-naphthylmethyl)-, diethyl ester (8CI) (CA INDEX NAME)



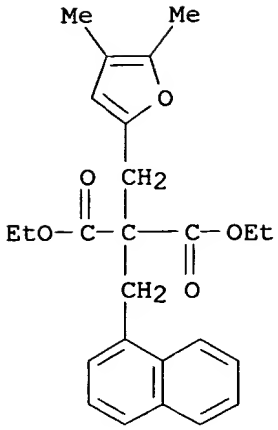
RN 25379-10-6 CAPLUS
CN Malonic acid, [5-(p-methoxybenzyl)furfuryl](1-naphthylmethyl)-, diethyl ester (8CI) (CA INDEX NAME)



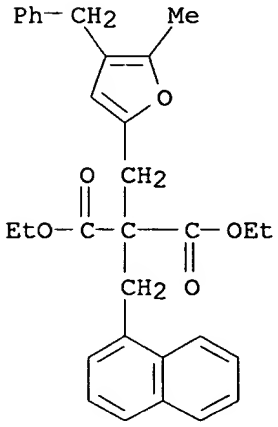
RN 25379-11-7 CAPLUS
CN Malonic acid, (1-naphthylmethyl)(5-veratrylfurfuryl)-, diethyl ester (8CI) (CA INDEX NAME)



RN 25379-24-2 CAPLUS
CN Malonic acid, (4,5-dimethylfurfuryl)(1-naphthylmethyl)-, diethyl ester (8CI) (CA INDEX NAME)



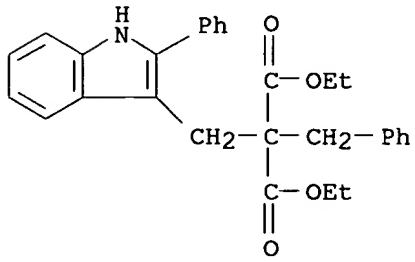
RN 25379-25-3 CAPLUS
CN Malonic acid, (4-benzyl-5-methylfurfuryl)(1-naphthylmethyl)-, diethyl ester (8CI) (CA INDEX NAME)



L5 ANSWER 55 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1969:524108 CAPLUS
DN 71:124108
TI 2-Phenylindol-3-yl methylation of methylene-active compounds
AU Buchmann, Gerhard; Voeltzke, W.
CS Tech. Hochsch. Chem. "Carl Schorlemmer", Leuna/Merseburg, Fed. Rep. Ger.
SO Pharmazie (**1969**), 24(8), 446-50
CODEN: PHARAT; ISSN: 0031-7144
DT Journal
LA German
GI For diagram(s), see printed CA Issue.
AB H2C(CO2Et)2 (6.4 g.) was treated with 0.8 g. Na in PhMe, 11.5 g. 3-(trimethylam-moniomethyl)-2-phenylindole methylsulfate added, and the mixture kept 2 hrs. at room temperature, 8 hrs. at 100°, and 110° until the reaction was complete, to give 57.5% I (R = H), m. 85°. The following I were similarly prepared (R, % yield, and m.p. given): Me, 15, 152°; Et, 36, 147°; Pr, 61, 162°; PhCH2, 55,

131°. Similarly prepared were the following II (R, R1, % yield, and m.p. given): H, CN, 81.7, 131°; Et, Ac, 49, 174°.
Treatment of I (R = H) with NaOEt gave 53% 2-phenylindole together with EtO(CH2)2CO2Et.

IT **23999-48-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 23999-48-6 CAPLUS
CN Malonic acid, benzyl[(2-phenylindol-3-yl)methyl]-, diethyl ester (8CI) (CA INDEX NAME)



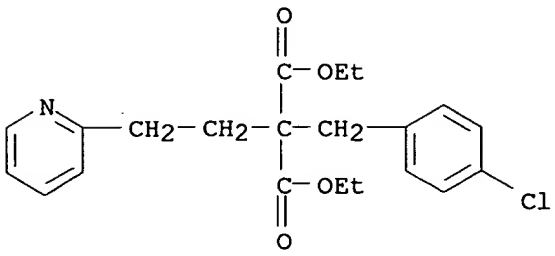
L5 ANSWER 56 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1968:78157 CAPLUS
DN 68:78157
TI Quinolizidine derivatives
IN Matsuo, Ichiro; Ohki, Sadao
PA Chugai Pharmaceutical Co., Ltd.
SO Jpn. Tokkyo Koho, 2 pp.
CODEN: JAXXAD
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 42008626	B4	19670418	JP	19640917 <--

GI For diagram(s), see printed CA Issue.
AB Na (2.2 g.) is added to a solution of 26 g. diethyl 2-(2-pyridyl)ethylmalonate in 200 ml. PhMe, the mixture heated at 110-15° for 10 hrs., 0.2 g. KI added, 17 g. p-chlorobenzyl chloride (I) added, the mixture heated 10 hrs. more, cooled, and filtered, the filtrate concentrated in vacuo and distilled in vacuo to remove unreacted I, the residue passed through a column of Al2O3 using C6H6-Me2CO (10:1), and the resulting solution evaporated to give 27.2 g. diethyl α-(p-chlorobenzyl) 2-(2-pyridyl)ethylmalonate (II), sirup. A solution of 19.5 g. II in 100 ml. AcOH is subjected to catalytic reduction using 1 g. PtO2, the mixture filtered, the filtrate concentrated, the residue dissolved in H2O, K2CO3 paste added and extracted with C6H6, the C6H6 extract concentrated, and the residue heated at 150-80° and distilled in vacuo to give 14 g. 3-carboethyoxy-3-(p-chlorobenzyl)-4-oxoquinolizidine (III), b0.2 185-95°, useful as an intermediate for the manufacture of 3-(p-chlorobenzyl)quinolizidine, useful as a uterus-contracting agent.

IT **17394-89-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 17394-89-7 CAPLUS

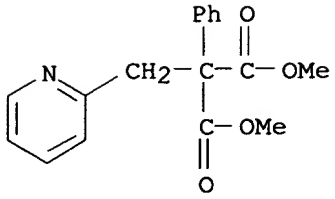
CN Malonic acid, (p-chlorobenzyl)[2-(2-pyridyl)ethyl]-, diethyl ester (8CI) (CA INDEX NAME)



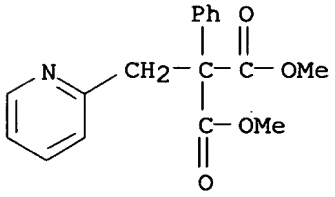
L5 ANSWER 57 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1967:37950 CAPLUS
DN 66:37950
TI Indolizine derivatives
IN Mohrbacher, Richard J.
PA McNeil Laboratories, Inc.
SO U.S., 6 pp. Division of U.S. 3245990
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3268535		19660823	US	19650614 <--

GI For diagram(s), see printed CA Issue.
AB Division of U.S. 3,245,990 (CA 64, 19563e). Title compds. where R is H or Ph and R1 is Ph or hydroxyalkyl were prepared by treating an indolizinecarboxylic acid ester or the acid chloride with substituted piperazines. Thus, a mixture of 5 parts Na octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate, 2.6 parts oxallyl chloride, and 5 parts 1-phenylpiperazine was stirred at room temperature for 2 hrs., washed with dilute HCl, and dried to give ocrahydro-3-oxo-1-phenyl-2-(4-phenyl-1-piperazinylcarbonyl)indolizine, m. 164-5° (EtOAc). Other I prepared were (R, R1, and m.p. given): H, Ph, 162-4° (EtOAc); and Ph, HOCH2CH2, 179-80° (EtOAc). I are useful as anti-inflammatory and hypotensive agents.
IT **3285-58-3P 3550-58-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 3285-58-3 CAPLUS
CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester (7CI, 8CI) (CA INDEX NAME)



RN 3550-58-1 CAPLUS
CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L5 ANSWER 58 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1967:2475 CAPLUS
DN 66:2475
TI Octahydro-3-oxoindolizines
IN Mohrbacher, Richard J.
PA McNeil Laboratories, Inc.
SO U.S., 6 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3274202		19660920	US	19630402 <--

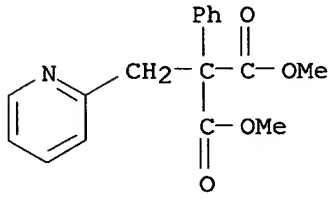
GI For diagram(s), see printed CA Issue.
AB Compds. of structure I were prepared Some of the products exhibited hypotensive and central nervous system depressant activity. A Knoevenagel condensation of 2-pyridinecarboxaldehyde 107 with CH2(CO2-Me)2 145 in the presence of piperidine and BzOH yields dimethyl 2-pyridylmethylenemalonate (II) 180 parts, m. 83.5-4.5° (aqueous MeOH). The diethyl analog (III) is similarly prepared (81%), b0.5 157°; sulfate m. 100-1.5° (EtOH-Et2O). Treatment of II 125 with PhMgBr in C6H6-Et2O at 0-5° afforded dimethyl phenyl-2-pyridylmethylmalonate (IV) 81 parts as HCl salt, m. 175-8° (decomposition) (EtOH-Et2O); free base m. 97-8° (petr. ether-EtOAc). Reduction of III 10.8 over PtO2 0.8 in absolute EtOH-AcOH at
60 psi. gave ethyl octahydro-3-oxo-2-indolizine-carboxylate (V) 8.9 parts, b0.06 110-11°. The dimethyl analog (VI) was analogously prepared, b1 138-45°. Similarly IV afforded methyl octahydro-3-oxo-1-phenyl-2-

indolizinecarboxylate (VII) as an isomer mixture, m. 84-9° (petr. ether-EtOAc); treatment of octahydro-3-oxo-1-phenyl-2-indolizinecarboxylic acid (m. 166-7°) with CH_2N_2 afforded the methyl ester, m. 113.5-14.0° (petr. ether-EtOAc). The ir spectrum is very similar, but not identical to VII. Condensation of VII 29.6 and $PhCH_2Cl$ 25.3 with NaH in PhMe gave Me octahydro-3-oxo-2-benzyl-2-indolizinecarboxylate (VIII) 35.8 parts, b0.2 160°, and free acid 6.3 parts, m. 170° (decomposition). Saponification of VIII with NaOH in aqueous MeOH afforded the free acid (as isomer mixture), m. 149-53° (EtOAc); repeated recrystn. yielded one isomer, m. 166-7°. Saponification of V gave 72% of the corresponding acid, m. 123-4.5° (Et_2O-CH_2Cl_2). Hydrolysis of VIII 23 with 10% NaOH (aqueous EtOH) gave octahydro-3-oxo-2-benzyl-2-indolizinecarboxylic acid 16.9 parts, m. 177° (decomposition) (EtOAc). Reduction of VIII 10.6 with $LiAlH_4$ yielded octahydro-1-phenyl-2-indolizinemethanol (IX) 8.5 parts; fumarate m. 173-5° (decomposition) (iso-PrOH-Et_2O). Treatment of IX with MeI gave two methiodide fractions, one, an isomer mixture, m. 218.5-19.5° (EtOH); the other, a single isomer, m. 184-6°, with similar ir spectra. Octahydro-2-benzyl-2-indolizinemethanol-HCl (X), m. 235-7° (iso-PrOH), was similarly prepared from VIII. Octahydro-2-indolizinemethyl benzilate, m. 104-6° (n-heptane), was obtained from the corresponding amino alcohol and ethyl benzilate by transesterification; similarly IX yielded octahydro-1-phenyl-2-indolizinemethyl benzilate, m. 108-9° (hexane). Refluxing Na octahydro-3-oxo-2-indolizinecarboxylate 7.2 with 9.2 β-dimethylaminoethyl chloride in C_6H_6 24 hrs. yielded 2-dimethylaminoethyl octahydro-3-oxo-2-indolizinecarboxylate 7.3 parts, b0.35 155°; fumarate m. 130-115° (sic) (EtOH-Et_2O). Similarly prepared were: 2-dimethylaminoethyl octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate fumarate, m. 161-3° (iso-PrOH-Et_2O); (1-methyl-4-piperidyl) octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate fumarate, m. 174-6° (EtOH-Et_2O); octahydro-3-oxo-2-(4-phenyl-1-piperazinylcarbonyl)indolizine, m. 162-4° (EtOAc); octahydro-3-oxo-2-[N-(2-dimethylaminoethyl)carbamoyl]indolizine, b0.35 174° [HCl salt m. 174-6° (iso-PrOH-Et_2O)]; octahydro-3-oxo-2-[N-(α-methylphenethyl)carbamoyl]indolizine, b0.075 185-92°. Preparing the acid chlorides from the corresponding Na salts and $(COCl)_2$ followed by reaction with the appropriate amine afforded: octahydro-3-oxo-2-[N-(3-pyridylmethyl)carbamoyl]indolizine, m. 115-16.5° (EtOAc-Et_2O); octahydro-3-oxo-1-phenyl-2-(1-pyrrolidinylcarbonyl)indolizine, m. 169-70° (EtOAc); octahydro-3-oxo-1-phenyl-2-(4-phenyl-1-piperazinylcarbonyl)indolizine, m. 164-5° (EtOAc); octahydro-3-oxo-1-phenyl-2-morpholinocarbonylindolizine, m. 128-9° (EtOAc); octahydro-3-oxo-1-phenyl-2-[4-(2-hydroxymethyl)-1-piperazinylcarbonyl]indolizine, m. 178-80° (EtOAc). Octahydro-1-phenyl-2-(1-pyrrolidinylmethyl)indolizine dihydrochloride, m. 245.5-7.0° (EtOH-Et_2O), was prepared by $LiAlH_4$ reduction of the corresponding oxo compound Analogously prepared were: octahydro-1-phenyl-1-morpholinomethylindolizine dihydrochloride, m. 270-2° (decomposition); octahydro-2-benzylindolizine, b0.15 97-100°; hexamate m. 108-120° (Me_2CO-Et_2O). Octahydro-3-oxo-2-benzyl-2-indolizinecarboxylic acid (XI) 70.6, yields on 10 min. heating as a melt 49.5 octahydro-3-oxo-2-benzylindolizine, b0.175 138°. Heating XI 4.5 with polyphosphoric acid 66 3 hrs. at 100° affords 1',5',6',7',8',8a'-hexahydro-1-oxospiro [indan-2,2' -indolizin] -3'(2'H)-one (XII) 4 parts, m. 121-2° (C_6H_{12}). Reduction of XII with $LiAlH_4$ gave octahydro-1-hydroxyspiro [indan-2,2'-indolizine], m.

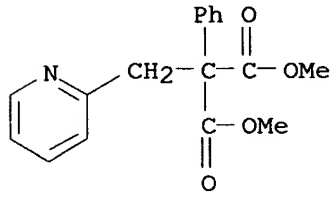
110-22° (C6H6-hexane). Reduction of XII 5.1 with NaBH4 in iso-PrOH yielded 1',5',6',7',8',8a'-hexahydro-1-hydroxyspiro[indan-2,2'-indolizine]-3'(2'H)-one 3.3 parts, m. 137-42°, and m. 151-5° (C6H12); the mother liquor yielded an addnl. 0.2 part second isomer; a mixed m.p. with the isomeric mixture was depressed.

IT **3285-58-3P 3550-58-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 3285-58-3 CAPLUS
CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester (7CI, 8CI) (CA INDEX NAME)



RN 3550-58-1 CAPLUS
CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L5 ANSWER 59 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1966:482196 CAPLUS
DN 65:82196
OREF 65:15351d-h,15352a-c
TI Octahydro-3-oxo-2-indolizinecarboxylic acids
IN Mohrbacher, Richard J.
PA McNeil Laboratories, Inc.
SO 6 pp.
DT Patent
LA Unavailable
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3268540		19660823	US	19650614 <--

GI For diagram(s), see printed CA Issue.
AB Compds. of the general formula I, where R1 is H or PhCH2 and R2 is CO2H, CH2OH, or a carbamoyl or a carboalkoxy group, are prepared and can be used

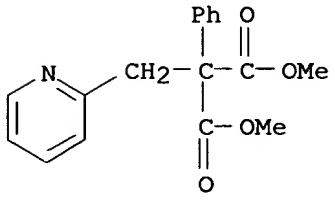
as hypotensive and antiinflammatory agents. Thus, a mixture of 107 parts 2-pyridinecarboxaldehyde, 145 parts CH2(CO2Me)2, 8 parts piperidine, 6.6 parts BzOH, and C6H6 is heated to give to give di-Me 2-pyridylmethylenemalonate (II), m. 83.5-4.5° (aqueous MeOH). Similarly prepared is di-Et 2-pyridylmethylenemalonate sulfate (III sulfate), m. 100-1.5° (EtOH-Et2O). A solution of PhMgBr (196 parts PhBr and 30 parts Mg) in Et2O is treated with a C6H6 solution of 125 parts II to give di-Me phenyl(2-pyridylmethyl)malonate, m. 97-8° (ligroine-EtOAc); HCl salt m. 175-8° (decomposition) (EtOH-Et2O). Similarly prepared is di-Et phenyl(2-pyridylmethyl)malonate, m. 71.5-2° (ligroine). III (10.8 parts) in a mixture of 100 parts EtOH and 4 parts HOAc is hydrogenated in the presence of 0.8 part Pt oxide to give 6.2 parts Et octahydro-3-oxo-2-indolinecarboxylate (IV), b0.06 110-11°. Similarly prepared are the following I (R1 = H; R, R2, and m.p. given): H, CO2Me, -- (b1 138-45°); Ph, CO2Me, 84-9° (ligroine-EtOAc). A solution of 29.6 parts I(R = R1 = H, R2 = CO2Me) in 50 parts PhMe is treated with 8.3 parts 54.7% NaH in mineral oil to give 15% I(R = H, R1 = PhCH2, R2 = CO2H), m. 170°, and I(R = H, R1 = PhCH2, R2 = CO2Me), b0.2 160°. A mixture of 35 parts I(R = Ph, R1 = H, R2 = CO2Me), 5 parts NaOH, and aqueous MeOH is refluxed to give I (R = Ph, R1 = H, R2 = CO2H) (V), m. 166-7° (EtOAc). I (R = Ph, R1 = H, R2 = CO2Me) (10.6 parts) is treated with 6.9 parts LiAlH4 to give I (R = Ph, R1 = H, R2 = CH2OH); fumarate m. 173-5° (decomposition) (iso-PrOH-Et2O); MeI salt, m. 218.5-19.5°. Similarly prepared is I (R = H, R1 = PhCH2, R2 = CH2OH) HCl salt, m. 235-7° (iso-PrOH). A mixture of 0.2 part NaOMe, 6.8 parts I (R = R1 = H, R2 = CH2OH), 700 parts n-heptane, and 10.6 parts Ph2C(OH)CO2Et is refluxed to give 6.8 parts I [R = R1 = H, R2 = CH2O2CC(OH)Ph2], m. 104-6° (heptane). Similarly prepared is I [R = Ph, R1 = H, R2 = CH2O2CC(OH)Ph2], m. 108-9° (hexane). V (6.8 parts) is treated with 1.05 parts NaOH to give I (R = Ph, R1 = H, R2 = CO2Na). Also prepared are the following I (R1 = H) (R, R2, and m.p. fumarate given): H, CO2CH2CH2NMe2, 113-15°; Ph, CO2CH2CH2NMe2, 161-3°; Ph, 1-methyl-4-piperidylcarbonyl, 174-6°; Ph, COCl, --. A mixture of 16.8 parts IV, a solution of 1.08 parts NaOMe in 165 parts MeOH, and 14.6 parts 4-phenylpiperazine is refluxed 28 hrs. to give 15.5 parts octahydro-3-oxo-2-(4-phenyl-1-piperazinylcarbonyl)indolizine, m. 162-4° (EtOAc). Also prepared are the following I (R1 = H) (R, R2, and m.p. given): H, CONHCH2CH2NMe2, -- (HCl salt m. 174-6°); H, CONHCHMeCH2Ph, -- (b0.075 185-92°); H, N-(3-pyridylmethyl)carbamoyl, 115-16.5°; Ph, 1-pyrrolidinylcarbonyl, 169-70°; Ph, 4-phenylpiperazinocarbonyl, 164-5°; Ph, morpholinocarbonyl, 128-9° (EtOAc); Ph, 4-(2-hydroxyethyl)piperazinocarbonyl, 179-80° (EtOAc). I (R = Ph, R1 = H, R2 = pyrrolidinylcarbonyl) is treated with 4.1 parts LiAlH4 to give I (R = Ph, R1 = H, R2 = 1-pyrrolidinylmethyl)-2HCl m. 245.5-7° (EtOH ether). Similarly prepared is I(R = Ph, R1 = H, R2 = morpholinomethyl)-2HCl, m. 270-2° (decomposition). I (R = H, R1 = PhCH2, R2 = CO2H) (VI) (70.6 parts) is heated to give 49.5 parts I(R = R2 = H, R1 = PhCH2) (VII), b0.275 138°. VII (15 parts) is treated with 7.4 parts LiAlH4 to give octahydro-2-benzylindolizine hexamate, m. 108-20° (Me2CO-Et2O). A mixture of 4.5 parts VI and 66 parts polyphosphoric acid is heated 3 hrs. at 100° to give 2.8 parts 1',5',6',7',8',8a'-hexahydro-1-oxospiro(indan - 2,2'-indolizin)3'(2'H)-one (VIII), m. 121-2°. VIII (7.7 parts) is treated with 3.4 parts LiAlH4 to give 3 parts octahydro-1-hydroxyspiro(indan-2,2'-indolizine), m. 110-22° (C6H6-hexane). VIII (5.1 parts) in 50 parts iso-PrOH is added to 0.76 part NaBH4 in 125 parts iso-PrOH and the mixture refluxed 2 hrs. to give 2.4 parts 1',5',6',7',8',8a'-hexahydro- 1-hydroxyspiro(indan-2,2'-indolizin)-

3'(2'H)-one, m. 137-42° and 151-5°.

IT **3285-58-3**, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester
3310-07-4, Malonic acid, phenyl(2-pyridylmethyl)-, diethyl ester
3550-58-1, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride
(preparation of)

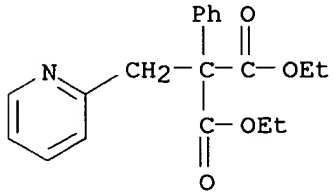
RN 3285-58-3 CAPLUS

CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester (7CI, 8CI) (CA INDEX NAME)



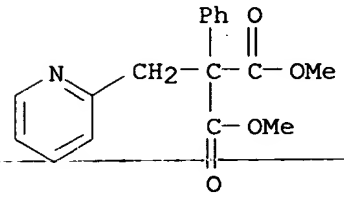
RN 3310-07-4 CAPLUS

CN Propanedioic acid, phenyl(2-pyridinylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 3550-58-1 CAPLUS

CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L5 ANSWER 60 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1966:104086 CAPLUS

DN 64:104086

OREF 64:19563e-h

TI 2-(Pyrrolidino and morpholino)carbonyl-3-oxooctahydroindolizines

IN Mohrbacher, Richard J.
PA McNeil Laboratories, Inc.
SO 6 pp.
DT Patent
LA Unavailable
FAN.CNT 1

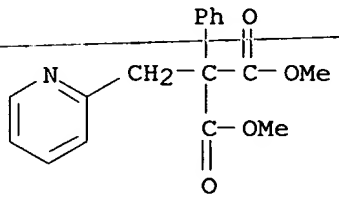
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3245990		19660412	US	19650614 <--

GI For diagram(s), see printed CA Issue.

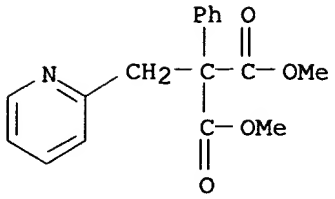
AB Dimethyl 2-pyridylmethylenemalonate (22.1 g.) in 150 ml. EtOH and 10 ml. AcOH in the presence of PtO2 was hydrogenated under 4 atmospheric H to give 14.3 g. methyl octahydro-3-oxo-2-indolizinecarboxylate (I, R = R1 = H, R2 = CO2Me), b1, 138-45°. A solution of 29.6 g. methyl octahydro-3-oxo-2-indolizinecarboxylate in 50 ml. PhMe was added during 15 min. to a suspension of 4.5 g. NaH in 250 ml. PhMe. Gas evolution stopped after refluxing 1 hr. A solution of 25.3 g. PhCH2Cl in 50 ml. PhMe was added to the stirred mixture at 100°. After 16 hrs. stirring at reflux the mixture gave 35.8 g. methyl octahydro-3-oxo-2-benzyl-2-indolizinecarboxylate (I, R = H, R1 = CO2Me, R2 = CH2Ph), b0.2 160°, and 6.3 g. octahydro-3-oxo-2-benzyl-2-indolizinecarboxylic acid (II), m. 170° (decomposition). During 20 min. 4.5 g. II was added to 66 g. polyphosphoric acid at 100°. After stirring 3 hrs. at 100° the mixture was worked up to give 4 g. III, m. 121-2° (cyclohexane). Also prepared were the following I (R, R1, R2, and m.p. or b.p.(mm.) given): H, CO2H, H, 123-4.5°; H, CO2H, CH2Ph, 177°; H, CO2Et, H, 110-11°(0.06); Ph, CO2H, H, 84-9°; H, CO2CH2CH2NMe2, H, 155°(0.35); Ph, 4-morpholinocarbonyl, H, 128-9°; Ph, 1-pyrrolidinylcarbonyl, H, 169-70°; H, CH2Ph, H, 138°(0.17). Also prepared was octahydro-2-benzyl-2-indolizinemethanol-HCl, m. 235-7°, and octahydro-1-phenyl-2-(1-pyrrolidinylmethyl)indolizine-2HCl, m. 245.5-47°. The indolizines of this patent have various pharmacol. activities, including hypotensive, antiinflammatory, and central nervous system depressant.

IT **3285-58-3**, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester
3550-58-1, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride
(preparation of)

RN 3285-58-3 CAPLUS
CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester (7CI, 8CI) (CA INDEX NAME)



RN 3550-58-1 CAPLUS
CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L5 ANSWER 61 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1966:93375 CAPLUS
DN 64:93375
OREF 64:17557b-h,17558a-c
TI Octahydroindolizines
IN Mohrbacher, Richard J.
PA McNeil Laboratories, Inc.
SO 6 pp.
DT Patent
LA Unavailable
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3245991		19660412	US	19630402 <--

GI For diagram(s), see printed CA Issue.

AB The title compds. (I), which possess hypotensive properties, antiinflammatory, and anticholinergic activity, were prepared, by the Knoevenagel condensation of 2-pyridinecarboxaldehyde (II) with a dialkyl malonate in the presence of a suitable condensing agent, and treating the resulting dialkyl 2-pyridylmethylenemalonate in a number of ways to produce the 1-Ph, and 2-PhCH2 substituted derivs. A mixture of 107 II, 145 CH2(CO2Me)2, 8 piperidine, and 6.6 parts BzOH was heated in C6H6 for 2.5 hrs. with azeotropie distillation of H2O to give 180 parts dimethyl 2-pyridylmethylenemalonate (III), m. 83.5-4.58° (aqueous MeOH). Similarly prepcd. was diethyl 2-pyridinemethylenemalonate (IV), IV sulfate m. 100-1.5°. To an ethereal solution of PhMgBr (prepared from 196 PhBr and 30 parts Mg) was added dropwise during 1.5 hrs. at 0° to 5° a C6H6 solution of 125 parts III. The mixture was poured into cold dilute HCl and the aqueous layer worked up to give 81 parts dimethyl phenyl-2-pyridylmethylmalonate (V), m. 97-8°, V.HCl m. 175-8°. IV similarly gave the corresponding diethyl phenyl-2-pyridylmethylmalonate (VI), m. 71.5-2°. VI (10.8 parts) was reduced over 0.8 part Pt oxide in 100 parts EtOH and 4 parts AcOH at 60 psi. of H to give 6.2 parts Et octahydro-3-oxo-2-indolizinecarboxylate (VII), b0.06 110-11°. III was similarly reduced to Me octahydro-3-oxo-2-indolizinecarboxylate (VIII), b1 138-45°. An ethanolic solution of 10 parts V containing 10 parts AcOH was hydrogenated at room temperature in the presence of 1 part Pt oxide at 51 psi. of H to give Me octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate (IX), m. 84-9° (IXa) and 113.5-14° (IXb). IXb was also obtained by treating octahydro-3-oxo-1-phenyl-2-indolizinecarboxylic acid (X), m. 166-7°, with CH2N2 in MeOH. A solution of 29.6 VIII in 50 PhMe was added dropwise during 15 min. to a suspension of NaH (8.3 parts 54.7% NaH in mineral oil) in 250 parts PhMe. The mixture was refluxed 1 hr. and

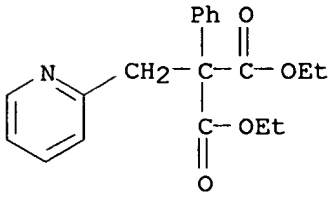
treated dropwise with stirring at 100° with 25.3 PhCH2Cl in 50 parts PhMe. The mixture was stirred 16 hrs. at reflux, cooled, carefully treated with 5 parts absolute EtOH and 100 parts H2O. The organic layer was worked up to give 6.3 parts octahydro-3-oxo-2-benzyl-2-indolizinecarboxylic acid (XI), m. 170° (with gas evolution), and 35.8 parts of the Me ester (XII) of XI, b0.2 160°. An aqueous methanolic solution of 35 parts IX containing 5 parts NaOH was refluxed 3 hrs. to give a mixture of geometrical isomers of the free acid (X). Octahydro-3-oxo-2-indolizinecarboxylic acid (XIII), m. 123-4.5° was similarly obtained from its Et ester (VII). A mixture of 2.3 XII, 40 EtOH, and 50 parts 10% NaOH was refluxed 5 hrs. to give 16.9 parts XI. IX was reduced with 6.9 parts LiAlH4 and the recovered product treated with 1.2 parts fumaric acid in MeOH to give I fumarate (R = Ph, R' = H, n = 1, R2= OH), m. 173-5° (decomposition). An ethereal solution of the above reduction product was treated with MeI for 50 hrs. to give the corresponding methiodide, m. 184-6° (one isomer), and m. 218.5-19.5° (mixture of isomers). XII was similarly reduced to I.HCl (R = H, R1 = PhCH2, n =1, R2 = OH), m. 235-7°. A suspension of 0.2 NaOMe, 6.8 I (R = R1 = H, n = 1, R2 = OH) (Ia), and 10.6 Et benzilate in 700 parts n-heptane was refluxed 1 hr. to give 6.8 parts I [R = R1 = H, n = 1, R2 = OCOC(OH)Ph2], m. 104-6°. Similarly prepared was I (R = Ph, R1 = H, n = 1, R2 = OCOC(OH)Ph2], m. 108-9°. A solution of 7.2 XIII and 1.6 NaOH in 50 parts H2O-EtOH was evaporated and the dry residue, resuspended in 50 parts C6H6, was treated with a C6H6 solution of Me2NCH2CH2Cl and refluxed 24 hrs. to give 2-dimethylaminoethyl octahydro-3-oxo-2-indolizinecarboxylate fumarate, m. 113-15°. Similarly prepared was 2-dimethylaminoethyl octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate fumarate, m. 161-3°. The acid chloride of X (prepared from 6.5 parts of the Na salt and 2.9 parts oxalyl chloride) was added dropwise to a solution of 3 parts 1-methyl-4-hydroxypiperidine in C6H6 and stirred 1 hr. at room temperature to give (1-methyl-4-piperidyl) octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate fumarate, m. 174-6°. The following were similarly prepared by the above procedures: octahydro-3-oxo-2-(4-phenyl-1-piperazinylcarbonyl) indolizine, m. 162-4°; octahydro-3-oxo-2-[N-(2-dimethylaminoethyl)carbamoyl]ind olizine, m. 174-6° (HCl salt); octahydro-3-oxo-2-[N-(α-methylphenethyl)carbamoyl]indolizine, b0.075 185-92°; octahydro-3-oxo-2-[N-(3-pyridylmethyl)carbamoyl]indolizine, m. 115-16.5°; octahydro-3-oxo-1-phenyl-2-(1-pyrrolidinylcarbonyl)indolizine, m. 169-70°; octahydro-3-oxo-2-(4-phenyl-1-piperazinyl-carbonyl)indolizine, m. 164-5°; octahydro-3-oxo-2-morpholino-carbonylindolizine, m. 128-9°; and octahydro-3-oxo-1-phenyl-2-[4-(2-hydroxymethyl)-1-piperazinylcarbonyl]indolizine, m. 179-80°. The following I derivs. were obtained by the procedures described above (R, R1, n, R2, and m.p. of the di-HCl salt given): Ph, H, 1, 1-pyrrolidinyl, 245.5-7°; and Ph, H, 1, morpholino, 270-2° (decomposition). XI (70.6 parts) was melted and heated 10 min. until no more gas evolved to give 49.5 parts octahydro-3-oxo-2-benzylindolizine (XIV), b0.175 138°. XIV (15 parts) was reduced in the usual manner with LiAlH4 and the recovered product converted to the hexamate salt of octahydro-2-benzylindolizine, m. 108-20°. XI (4.5 parts) was added portionwise during 20 min. to 66 parts polyphosphoric acid heated to 100°, and kept at 100° 3 hrs. with stirring to give 1',5',6',7',8',8'a-hexahydro-1-oxospiro(indan-2,2'-indolizin)-3'(2'H)-one (XV), m. 121-2°. XV was reduced with LiAlH4, as above to give octahydro-1-hydroxyspiro(indan-2,2'-indolizine), m. 110-22°. XV (5.1 parts) in 50 parts iso-PrOH was added rapidly

to a suspension of 0.76 part NaBH4 in 125 parts 2-PrOH and the mixture was refluxed 2 hrs. and worked up in the usual manner to give 2.4 parts 1',5',6',7',8',8'a-hexahydro-1-hydroxyspiro(indan-2,2'-indolizine)-3'(2'H)-one, m. 137-42° and m. 151-5°.

IT **3310-07-4**, Malonic acid, phenyl(2-pyridylmethyl)-, diethyl ester
3550-58-1, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride
(preparation of)

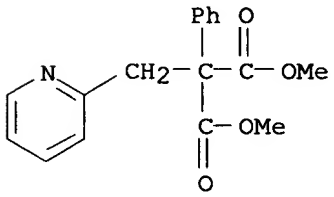
RN 3310-07-4 CAPLUS

CN Propanedioic acid, phenyl(2-pyridinylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 3550-58-1 CAPLUS

CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L5 ANSWER 62 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1965:462961 CAPLUS

DN ~~63:62961~~

OREF 63:11513b-h,11514a-d

TI Oxo- and hydroxyspiroindanindolizines

IN Mohrbacher, Richard J.

PA McNeil Laboratories, Inc.

SO 5 pp.

DT Patent

LA Unavailable

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3189611		19650615	US	19630402 <--

GI For diagram(s), see printed CA Issue.

AB Compds. of the general structure, in which R1 is H or oxo and R2 is H, oxo, OH, or OCOR, have hypotensive, antiedema, and antiinflammatory

activity. A mixture of 107 g. 2-pyridinecarboxaldehyde (I), 147 g. $CH_2(CO_2Me)_2$, 8 g. piperidine, and 6.6 g. BzOH in C_6H_6 heated 2.5 hrs. with azeotropic distillation of H_2O, concentrated, diluted with Et_2O, washed with $NaHCO_3$ and H_2O, dried, evaporated, and triturated with aqueous MeOH gave 180 g. 2-C_5H_4NCH:$C(CO_2Me)_2$ (II), m. 83.5-4.5° (aqueous MeOH). I and $CH_2(CO_2Et)_2$ similarly gave 81% 2-C_5H_4NCH:$C(CO_2Et)_2$ (III), b0.5 157°; sulfate m. 100-1.5° (EtOH-Et_2O). Addition of 125 g. II in C_6H_6 to PhMgBr (from 30 g. Mg and 196 g. PhBr) at 0-5° over 1.5 hrs., stirring 2 hrs. at 5°, pouring into dilute HCl, and partial neutralization of the aqueous layer with K_2CO_3 gave 81 g. 2-$C_5H_4NCH_2CPh(CO_2Me)_2$.HCl, m. 175-8° (decomposition) (EtOH-Et_2O); free base (IV) m. 97-8° (petroleum ether-EtOAc). III (51 g.) gave 35 g. 2-$C_5H_4NCH_2CPh(CO_2Et)_2$ (V), m. 71.5-72° (petroleum ether). Hydrogenation of 22.1 g. II on 1.25 g. PtO_2 in 150 ml. EtOH and 10 ml. HOAc gave 14.3 g. Me octahydro-3-oxo-2-indolizinecarboxylate (VI), b1 138-45°. Hydrogenation of 10.8 g. III gave 8.9 g. Et octahydro-3-oxo-2-indolizinecarboxylate (VII), b0.06 110-11°. Hydrogenation of 10 g. IV in EtOH and 10 ml. HOAc on 1 g. PtO_2 gave a mixture of isomers of Me octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate (VIII), m. 84-9° (petroleum ether-EtOAc). Action on 29.6 g. VI in 50 ml. PhMe by 4.5 g. NaH in 250 ml. PhMe, followed by 25.3 g. $PhCH_2Cl$ in 50 ml. PhMe 16 hrs. gave 6.3 g. octahydro-3-oxo-2-benzyl-2-indolizinecarboxylic acid (IX), m. 170° (gas evoln.) and 35.8 g. Me octahydro-3-oxo-2-benzyl-2-indolizinecarboxylate (X), b0.2 160°. Saponification of 35 g. VIII gave 29.3 g. mixed isomers of octahydro-3-oxo-1-phenyl-2-indolizinecarboxylic acid (XI) m. 149-53° (EtOAc). Several recrystns. of X from EtOAc gave a single geometrical isomer, white prisms, m. 166.7°. Saponification of VII gave a 72% yield of mixed isomers of octahydro-3-oxo-2-indolizinecarboxylic acid (XII), m. 110-21°, from which a pure isomer, m. 123-4.5° (Et_2O-CH_2Cl_2) was obtained. Saponification of 23 g. X by 50 ml. 10% NaOH and 40 ml. 95% EtOH and the mixture refluxed 5 hrs. gave 16.9 g. IX, m. 177° (gas evoln.) (EtOAc). Et octahydro-3-oxo 1-phenyl-2-indolizinecarboxylate (13.2 g.) and 8.2 g. $LiAlH_4$ in Et_2O were refluxed 3.5 hrs., treated with 24.5 ml. H_2O, filtered, dried ($MgSO_4$), and concentrated to give 8.5 g. oil, octahydro-1-phenyl-2-indolizinemethanol (XIII).

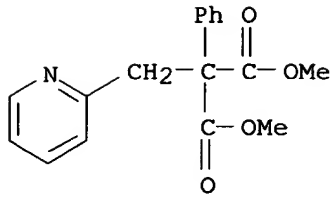
Treatment of this oil with 5 g. MeI 50 hrs. gave 7.3 g. solid, fractional crystallization of which from EtOH gave two isomers of octahydro-1-phenyl-2-indolizinemethanol methiodide, 4.1 g., m. 218.5-19.5°, and 0.8 g., m. 184-6°. Similar reduction of 10.6 g. VIII with 6.9 g. $LiAlH_4$, followed by treatment of the oil with fumaric acid in MeOH, gave octahydro-1-phenyl-2-indolizinemethanol fumarate, m. 173-5° (decomposition) (iso-PrOH-Et_2O). Reduction of 14.4 g. X by 5.7 g. $LiAlH_4$ and washing, drying, and concentration of the mixture, followed by HCl, gave octahydro-2-benzyl-2-indolizinemethanol hydrochloride, m. 235-7° (iso-PrOH). A mixture of 6.8 g. octahydro-2-indolizinemethanol, 0.2 g. NaOMe, and 10.6 g. Et benzilate in 700 ml. C_7H_{16} was refluxed 1 hr., concentrated, diluted with Et_2O, and extracted with dilute HCl to give 6.8 g. octahydro-2-indolizinemethyl benzilate, m. 104-6°. Similar treatment of 9 g. XIII with 9.5 g. Et benzilate gave octahydro-1-phenyl-2-indolizinemethyl benzilate, m. 108-9°. The Na salt from 7.2 g. XII was refluxed 24 hrs. in C_6H_6 solution of $Me_2NCH_2CH_2Cl$ to give 7.3 g. β-dimethylaminoethyl octahydro-3-oxo-2-indolizinecarboxylate, b0.35 155°; fumarate m. 113-15° (iso-PrOH-Et_2O). Similarly obtained was β-dimethylaminoethyl octahydro-3-oxo-1-phenyl-1-indolizinecarboxylate, oil; fumarate m. 161-3° (iso-PrOH-Et_2O). The acid chloride of XI (prepared from 6.5 g. XI Na salt and 2.9 g. $(COCl)_2$)

and 3 g. 1-methyl-4-hydroxypiperidine in C6H6 gave 1-methyl-4-piperidyl octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate, oil; fumarate m. 174-6° (EtOH-Et2O). 4-Phenylpiperazine (14.6 g.) added to 16.8 g. VII and 1.08 g. NaOMe in 165 ml. MeOH, and the mixture refluxed 28 hrs. gave 15.5 g. octahydro-3-oxo-2-(4-phenyl-1-piperazinylcarbonyl)indolizine, m. 162-4° (EtOAc). Similarly, 16.8 g. VII and 14 g. Me2NCH2CH2NH2 gave 9.5 g. octahydro-3-oxo-2-[N-(2-dimethylaminoethyl)carbamoyl]indolizin e, b0.35 174°; hydrochloride m. 174-6° (iso-PrOH-Et2O); and 19.7 g. VI and 15 g. (+)-amphetamine gave octahydro-3-oxo-2-[N-(α-methylphenethyl)carbamoyl]indolizine, b0.075 185-92°. XI acid chloride (from 8.1 g. XI and 5.6 g. (COCl)2) and 5.2 g. 3-aminomethylpyridine gave 5.5 g. octahydro-3-oxo-2-[N-(3-pyridylmethyl)carbamoyl]indolizine, m. 115-16.5° (EtOAc-Et2O). Similarly prepared were octahydro-3-oxo-1-phenyl-2-(1-pyrrolidinylcarbonyl)indolizine (XIV), m. 169-70° (EtOAc); octahydro-3-oxo-1-phenyl-2-(4-phenyl-1-piperazinylcarbonyl)indolizine, m. 164-5° (EtOAc); octahydro-3-oxo-1-phenyl-2-morpholinocarbonylindolizine (XV), m. 128-9° (EtOAc); and octahydro-3-oxo-1-phenyl2-[4-(2-hydroxymethyl)-1-piperazinylcarbonyl]indolizine, m. 179-80° (EtOAc). Action of 4.1 g. LiAlH4 on 6.6 g. XIV in Et2O 3 hrs., followed by 12 ml, H2O, filtration, concentration, drying, and dry HCl treatment gave octahydro-1-phenyl-2-(1-pyrrolidinylmethyl)indolizine dihydrochloride, m. 245.5-47° (EtOH-Et2O). Reduction of XV by LiAlH4, followed by HCl, gave octahydro-1-phenyl-2-morpholinomethylindolizine dihydrochloride, m. 270-2° (decomposition). Thermal decarboxylation of 70.6 g. IX gave 49.5 g. octahydro-3-oxo-2-benzylindolizine, pale yellow-oil, b0.175 138°, reduction of which by LiAlH4 gave octahydro-2-benzylindolizine, b0.15 97-100°; hexamate m. 108-20° (Me2COEt2O). A mixture of 4.5 g. IX and 66 g. polyphosphoric acid at 100° 3 hrs., poured onto crushed ice, and extracted with Et2OC6H6, gave 4 g. 1',5',6',7',8',8' α-hexahydro-1-oxospiro(indan-2,2'-indolizine)-3'(2'H)-one (XVI), m. 121-2° (cyclohexane). LiAlH4 (3.4 g.) and 7.7 g. XVI in 900 ml. Et2O, refluxed 20 hrs., cooled, mixed with 10.4 ml. H2O, filtered, extracted with 10% NaOH, washed, dried, and concd, gave 5.6 g. octahydro-1-hydroxyspiro(indan-2,1'-indolizine), m. 110-22° (C6H6-C6H14). Reduction of 5.1 g. XVI in 50 ml. iso-PrOH by 0.76 g. NaBH4 in 125 ml. isoPrOH in 2 hrs. refluxing, followed by 125 ml. 2.9M HCl, concentration, extraction with Et2O-C6H6, gave 3.8 g. oil; and an addnl. 0.6 g. oil was obtained by adding 35% NaOH to the aqueous layer, extracting with CH2Cl2, and concentrating Recrystn. of the oil, first from C6H6-C6H14, then from cyclohexane-C6H14 then from cyclohexane ultimately gave 0.2 g. of a single isomer of 1',5',6',7',8',8' α-hexahydro-1-hydroxyspiro(indan-2,2'-indolizine)-3'(2'H)-one, m. 154-6°.

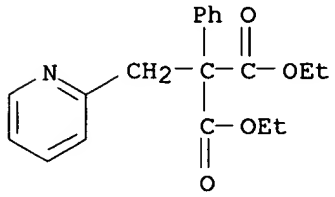
IT **3285-58-3**, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester
3310-07-4, Malonic acid, phenyl(2-pyridylmethyl)-, diethyl ester
3550-58-1, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride
(preparation of)

RN 3285-58-3 CAPLUS

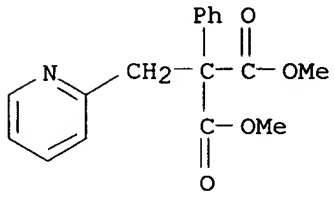
CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester (7CI, 8CI) (CA INDEX NAME)



RN 3310-07-4 CAPLUS
CN Propanedioic acid, phenyl(2-pyridinylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 3550-58-1 CAPLUS
CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L5 ANSWER 63 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1965:82624 CAPLUS
DN 62:82624
OREF 62:14694e-h,14695a-c
TI Barbituric acid derivatives
IN Wiggins, Leslie F.; James, John W.; Gittos, Maurice W.
PA Aspro-Nicholas Ltd.
SO 9 pp.; Division of Brit. 976,551
DT Patent
LA Unavailable
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 977321		19641209	GB	19591217 <--

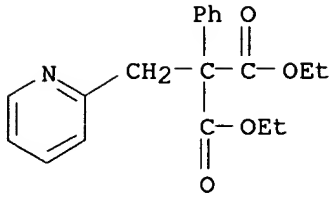
GI For diagram(s), see printed CA Issue.

AB The title compds. (I) are prepared by condensation of a chloramine with a monosubstituted malonic ester to form a basic disubstituted malonic ester, R1R2C(CO2Et)2 (Ia) which is then condensed with urea or thiourea to give the I. Thus, a solution of 55 g. di-Et 2-phenylmalonate and 5.7 g. NaH in 150 ml. dry dioxane was stirred until effervescence ceased. The mixture was heated at 80° and 29 g. of 2-dimethylaminoethyl chloride added dropwise. After refluxing and stirring 3 hrs. the mixture was cooled, washed with ether and the aqueous layer acidified. Ether extraction of the acidic layer and distillation gave di-Et 2-(2-dimethylaminoethyl)-2-phenylmalonate (II), b0.001 118-24°. Treatment of II with Na in dry EtOH gave 5-(2-dimethylaminoethyl)-5-phenylbarbituric acid-HCl, m. 284-6°. Similarly prepared was di-Et 2-(2-pyridylmethyl)-2-phenylmalonate-HCl (III), m. 166-8°. Hydrogenation of III with PtO as catalyst gave di-Et 2-(2-piperidinylmethyl)-2-phenylmalonate-HCl (IV), m. 174-5°. Treatment of IV with HCO2H, HCO2Na and 37-41% HCHO in H2O gave di-Et 2-(N-methyl-2-piperidylmethyl)-2-phenylmalonate (V), b0.15 140-7°. Treatment of V with thiourea and Na in anhydrous MeOH gave 5-(N-methyl-2-piperidylmethyl)-5-phenyl-2-thiobarbituric acid, m. 231-2°, (HCl salt m. 216-20°). Similarly prepared was 5-sec-amyl-5-(2-dimethylaminoethyl)-2-thiobarbituric acid-HCl, m. 265°. Treatment of 5-(2-diethylaminoethyl)-5-phenyl-2-thiobarbituric acid with 2.5N HNO3 gave 5-(2-diethylaminoethyl)-5-phenylbarbituric acid, m. 193-4°. A MeOH solution of the free base of III was stirred with Na and thiourea in MeOH to give 5-(2-pyridylmethyl)-5-phenyl-2-thiobarbituric acid, m. 268°, which on treatment with 2.5N HNO3 gave 5-(2-pyridylmethyl)-5-phenylbarbituric acid (VI), m. 320°. Hydrogenation of VI (PtO) gave 5-(2-piperidylmethyl)-5-phenylbarbituric acid-HCl, m. 197-9°, which refluxed with H2O, HCO2H, HCO2Na, and 37-41% aqueous HCHO gave 5-(N-methyl-2-piperidylmethyl)-5-phenylbarbiturie acid-HCl hydrate, m. 195-200°. Treatment of 5-(2-dimethylaminoethyl)-5-(m-methoxyphenyl)-2-thiobarbiturie acid in refluxing HOAc and concentrated HBr gave, after neutralization and treatment with HCl, 5-(2-dimethylaminoethyl)-5-(m-hydroxyphenyl)-2-thiobarbituric acid-HCl (VII), m. 270°. The oxo-analog, prepared as VI m. 269-71°. Similarly to II was prepared di-Et 2-(2-dimethylaminopropyl)-2-phenylmalonate, b0.1 116-20°, (H oxalate m. 144-6°). The malonates and barbiturates prepd are given in the table. Treatment of thiourea dissolved in a solution of Na in anhydrous EtOH with di-Et 2-(2-diethylaminoethyl)-2-phenylmalonate gave 5-(2-diethylaminoethyl)-5-phenyl-2-thiobarbituric acid, m. 215° (HCl salt m. 234-6°). Similarly prepared was 5-(2-dimethylaminoethyl)-5-(o-chlorophenyl)-2-thiobarbituric acid, m. 236-8° (HCl salt m. 287-88°). These compds. are active in suppressing tremorine induced spasms in mice.

IT **1454-12-2**, Malonic acid, phenyl(2-pyridylmethyl)-, diethyl ester, hydrochloride
(preparation of)

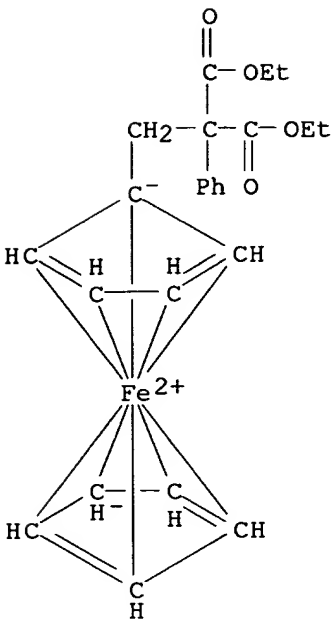
RN 1454-12-2 CAPLUS

CN Propanedioic acid, phenyl(2-pyridinylmethyl)-, diethyl ester, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L5 ANSWER 64 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1964:440531 CAPLUS
DN 61:40531
OREF 61:7041d-g
TI Heterobridged ketones derived from ferrocene
AU Gautheron, Bernard; Triouflet, Jean
CS Fac. Sci., Dijon, Fr.
SO Compt. Rend. (**1964**), 258(26), 6443-5
DT Journal
LA Unavailable
GI For diagram(s), see printed CA Issue.
AB In this abstract Z = ferrocenyl radical (C5H5FeC5H4-). The sodio derivative of a substituted Et malonate, RCH(CO2Et)2, was prepared in xylene, powdered [ZCH2NMe3]+ I- was added, and the product, ZCH2CR(CO2Et)2, was isolated by chromatog. on Al2O3 [R = Me (I), m. 62°; R = Ph (II), m. 81°]. I was saponified to form ZCH2CHMe(CO2H)2, decomposed 198°, which was decarboxylated to give ZCH2CHMeCO2H (III), m. 112°; II similarly gave directly ZCH2CHPhCO2H (IV), m. 98°. III or IV with (CF3CO)2O gave V (R = Me m. 102°; R = Ph m. 186°). The structures of the heterobridged ketones were established by mass, IR, and UV spectroscopy. The influence of the gem dialkyl group in promoting the latter reaction is attributed to steric effects. Polarog. measurements on the ketones did not show the expected inhibition of resonance of CO.
IT **33111-48-7**, Iron, cyclopentadienyl[(β,β-dicarboxyphenethyl)cyclopentadienyl]-, diethyl ester
(preparation of)
RN 33111-48-7 CAPLUS
CN Ferrocene, [3-ethoxy-2-(ethoxycarbonyl)-3-oxo-2-phenylpropyl]- (9CI) (CA INDEX NAME)



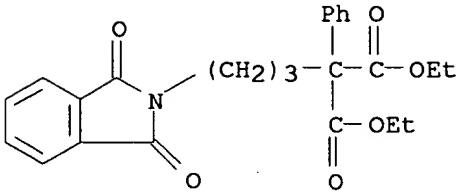
L5 ANSWER 65 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1964:404074 CAPLUS
DN 61:4074
OREF 61:608e-h,609a
TI α,α-Disubstituted diacids and their derivatives. XVII. δ-Amino-α-phenylpentanoic acids
AU Salmon-Legagneur, F.; Neveu, C.
CS Ecole Natl. Super. Chim., Rennes
SO Bulletin de la Societe Chimique de France (**1963**), (10), 2175-89
CODEN: BSCFAS; ISSN: 0037-8968
DT Journal
LA Unavailable
OS CASREACT 61:4074
GI For diagram(s), see printed CA Issue.
AB cf. CA 59, 6300h. Benzyl cyanide derivatives (0.2 mole) were refluxed with 0.225 mole NaNH2 in 300 ml. C6H6, cooled, and refluxed 3-4 hrs. with 0.20 mole γ-bromopropylphthalimide in 20 ml. HCONMe2. After dilution with H2O, Et2O extraction, and evaporation, I was obtained (R, m.p., and % yield given): H, 110°, 62; Ph, 173-4°, 75; PhCH2, 108°, 73; PhCH2CH2, 109°, 72; Et, 83°, 59; Pr, 90-1°, 58; Bu, 80°, 55.5; cyclohexyl, 131°, 54. Similarly, II was prepared (same data): H, 89-90°, 77; Ph, 125°, 76; PhCH2, 98°, -; Et, 80°, 45; Pr, 117°, 45; Bu, 77°, 48; C6H11, 114-15°, -. I or II(0.1 mole) refluxed a week in 200 ml. 66% HBr and 100 ml. AcOH gave PhCR(CO2H)CH2CH2CH2NH2.HBr (III) (same data): Ph, 260°, 90-95; PhCH2, 174°, 82; PhCH2CH2, 214°, 72; Et, 161°, 74-95; Pr, 178°, 72-90; Bu, 199-201, 68-80. III dissolved in H2O and treated with 10% NaOH to pH 7-9 gave the free amino acids (IV) (R and m.p. given): H, 280°; Ph, 240°; PhCH2, 290° (decomposition); PhCH2CH2, 150-5° (decomposition); Et, 269°; Pr, 250°; Bu, 181° and 290°. IV heated

above its m.p. furnished V (R and m.p. given): H, 173°; Ph, 189-90°; PhCH2, 134°; PhCH2CH2, 127-8°; Et, 124°; Pr, 102°; Bu, 69-74°; cyclohexyl, 179-80°. IV dissolved in Ae2O, evaporated, and diluted with H2O gave V N-Ac derivs. (VI) (same data): H, 45-6°; Ph, 94°; PhCH2, 83°; PhCH2CH2, 60-1°: Et, 106-7°. VI dissolved in EtOH and alkalinized afforded V. V (R = Ph) treated with NaNH2 in C6H6 and then refluxed 2-3 hrs. with MeI gave N-Me derivative of V (R = Ph), m. 119-20°; similarly, V(R = PhCH2)gave the N-Me derivative, m. 86°. V(R = Et) with PhCH2Cl gave N-benzyl derivative, m. 54-5°. Ethyl phenylmalonate (0.1 mole) refluxed 1 hr. with 2.3 g. Na in EtOH, cooled, and treated with γ-bromopropylphthalimide in 20 ml. HCONMe2 and then refluxed again 4 hrs. gave Et 2-phthalimidopropyl-2-phenylmalonate (VII), m. 90°. VII refluxed with 48% HBr gave 5-phthalimido-2-phenylpentanoic acid, m. 162°. VII refluxed with 48% HBr in AcOH 60 hrs. furnished III (R = H), m. 130°. II (10 g.) (R = Ph) refluxed 3 hrs. with 30 ml. NH2NH2.H2O in 100 ml. EtOH gave 86% 5-amino-2,2-diphenylpentanenitrile, b2 195-200°.

IT **96465-03-1**, Malonic acid, phenyl(3-phthalimidopropyl)-, diethyl ester
(preparation of)

RN 96465-03-1 CAPLUS

CN Malonic acid, phenyl(3-phthalimidopropyl)-, diethyl ester (7CI) (CA INDEX NAME)



L5 ANSWER 66 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1963:409293 CAPLUS

DN 59:9293

OREF 59:1747f-h

TI α-Substituted δ-aminopentanoic acid

AU Salmon-Legagneur, Francois; Neveu, Cecile

CS Fac. Sci., Rennes, Fr.

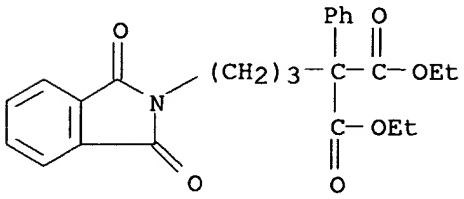
SO Compt. Rend. (**1963**), 256, 187-9

DT Journal

LA Unavailable

AB NH2(CH2)3CPhRCO2H (I) was prepared as the HBr salt by condensing PhRCNaCN with bromopropyl-phthalimide in HCONMe2, and refluxing the resulting 5-phthalimido-2-phenyl-2-alkylvaleronitrile (yields 55-95%) in 66% aqueous HBr and AcOH (yields 75-90%). The free amino acid was obtained by neutralizing with NaOH. The lactams were also prepared by heating the corresponding amino acid. The following I were prepared (R, and m.p. of I, the HBr salt, and the lactam given): H, 280°, 130°, 173°; Et, 269°, 161°, 124°; Pr, 204°, 178°, 102°; Bu, 295°, 199-201°, -- (the lactam was not obtained); Ph, 240°, 260°, 189-90°; PhCH2, 290°, 174°, 134°; PhCH2CH2, 150-55° (decomposition), 214°, 127-8°.

IT **96465-03-1**, Malonic acid, phenyl(3-phthalimidopropyl)-, diethyl ester
(preparation of)
RN 96465-03-1 CAPLUS
CN Malonic acid, phenyl(3-phthalimidopropyl)-, diethyl ester (7CI) (CA INDEX NAME)



L5 ANSWER 67 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1963:8783 CAPLUS
DN 58:8783
OREF 58:1435d-h
TI α-Substituted carboxylic acids
IN LIPHA; Szarvasi, Etienne; Newvy, Liliane; Fontaine, Louis
PA Lyonnaise Industrielle Pharmaceutique
SO 40 pp.
DT Patent
LA Unavailable

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI BE 613547		19620806	BE		<--
FR AD81162			FR		
PRAI FR		19620223			

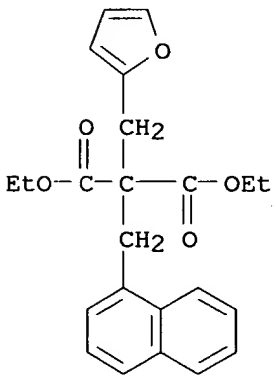
AB Compds. of the general formula RR'CHOR'' (I), where COR'' can be an acid, ester, acid salt, or amide group, can be used to induce cholesterolemia; they have choleretic properties. Na (9 g.) is placed in 256 ml. absolute EtOH, 96 g. Et furfurylmalonate added, the mixture boiled 5 min., cooled, 70.4 g. 1-C10H7CH2Cl added dropwise, the mixture refluxed 24 hrs., extracted with C6H6, and the extract distilled to give 69% Et α-(1-naphthylmethyl)-α-furfurylmalonate, b1.5 202-3°. Similarly prepared is Et (1-naphthylmethyl)tetrahydrofurfurylmalonate, b0.95 211°. C10H7CH2CN is refluxed with NaNH2 and furfuryl chloride 6 hrs. to give α-(1-naphthyl)-α-furfurylacetonitrile, b2 194-5°, n22D 1.611, m. 46-8° (EtOH-C6H14). Similarly prepared are the following RR'CHCN (R-,R', b.p. given): 1-C10H7, tetrahydrofurfuryl, b0.4 154°; 1-C10H7, 3-tetrahydrofurfuryl, propyl, b0.4 183°; 1-C10H7, MeCH:CHCH2, b0.9 138°; 1-C10H7, H2C:CHCH2, b0.4 130°, n19.5D 1.603, d21 1.0520. I prepared were [R, R', R'', and phys. properties given]: 1-C10H7CH2, furfuryl, OH, m. 72-4°, b1.5 207-9° (Na salt m. 260-2°); 1-C10H7CH2, furfurylmethyl, OMe, b2 193-5°, d25 1.1333, n23D 1.583; 1-C10H7CH2, furfuryl, tert-BuCH2O, b2 179-80°, n23.5D 1.5585; 1-C10H7CH2, furfuryl, OCH2CH2NEt2, b1 188-90°, n21D 1.5728; 1-C10H7CH2, 3-tetrahydrofurfurylpropyl, OH, b1 220-2° (Na salt m. 261°); 1-C10H7CH2, 3-tetrahydrofurfurylpropyl, OMe, b0.6 178°, d24 1.182; 1-C10H7, furfuryl, OH, b2 218-19°, m. 80-2° (Na salt m. 302-3°); 1-C10H7, furfuryl, NH2, m. 107-8° (EtOH); 1-C10H7, furfuryl, OMe, b0.7 158°, d24 1.1375, n23D 1.596; 1-C10H7,

furfuryl, tert-BuCH2O, b1 171-2°, n21D 1.561; 1-C10H7, furfuryl, OCH2CH2NEt2, b1.5 215-16°, n24D 1.5745; 1-C10H7, furfuryl, NHCH2CH2OH, m. 122-3° (EtOAc and EtOH); 1-C10H7, tetrahydrofurfuryl, OH, b1.5 217-18°, m. 135° (EtOH-C6H14) (Na salt m. 250-1°); 1-C10H7, tetrahydrofurfuryl, NH2, m. 153-3.5° (EtOAc); 1-C10H7, tetrahydrofurfuryl, OMe, b0.36 157-8°; 1-C10H7, tetrahydrofurfuryl, tert-BuCH2O, b1 182-5°; 1-C10H7, tetrahydrofurfuryl, OCH2CH2NEt2, b0.36 191°; 1-C10H7, 3-tetrahydrofurylpropyl, OH, b0.35 210°; 1-C10H7, 3-tetrahydrofurfurylpropyl, O(CH2)2NEt2, b0.6 216°, n22D 1.5555; 1-C10H7CH2, tetrahydrofurfuryl, OH, b1 212°; 1-C10H7, MeCH:CHCH2,OH, b0.7 167°; 1-C10H7, MeCH:CHCH2, NH2, m. 121-2° (EtOAc); 1-C10H7, MeCH:CHCH2, OMe, b1 131-4° d22 1.0616, n22D 1.5825; 1-C10H7, MeCH:CHCH2, O(CH2)2NEt2, b2 197°, d22 1.020, n22D 1.564; 1-C10H7, MeCH:CHCH2, NHNH2, m. 125-7° (EtOAc), sublimation at 100°; 1-C10H7, H2C:CHCH2, OH, b0.6 157-8°; 1-C10H7, H2C:CHCH2, O(CH2)2NEt2, b1 148-9°, d23 1.0205, n24D 1.555; 1-C10H7, H2C:CHCH2, O(CH2)2NMe2, b1 166-8°.

IT **95432-29-4**, Malonic acid, furfuryl(1-naphthylmethyl)-, diethyl ester
(preparation of)

RN 95432-29-4 CAPLUS

CN Propanedioic acid, (2-furanylmethyl)(1-naphthalenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 68 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1962:483159 CAPLUS

DN 57:83159

OREF 57:16563d-i

TI α-Substituted carboxylic acids

IN Szarvasi, Etienne; Neuvy, Liliane

PA LIPHA; Lyonnaise Industrielle Pharmaceutique

SO 29 pp.

DT Patent

LA Unavailable

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI FR 1289597		19620406	FR	19610223	<--
GB 999589			GB		
GB 999590			GB		
US 3257420		1966	US		<--

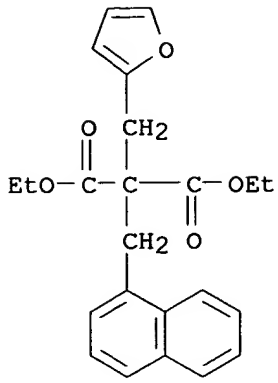
US 3282964 1966 US <--
US 3282965 1966 US <--

AB The Na salts, esters, and amides of R'R''C(CO2R)2 (I), RCH2CHR'CN (II), and R'R''CHCO2R (III) show choleretic and hypocholesterolemic properties. NaOEt (9 g.) in 256 ml. absolute EtOH is prepared, 96 g. ethyl furfurylmalonate added, the mixture boiled 5 min., cooled, 70.4 g. 1-chloromethylnaphthalene added dropwise, the mixture refluxed 24 hrs., extracted with C6H6, and distilled to give 105 g. I (R = Et, R' = furfurylmethyl, R'' = 1-C10H7CH2), b1.5 202-3°. Similarly prepared are: I [R = Et, R' = 3-(tetrahydrofurfuryl)propyl, R'' = 1-C10H7CH2], b0.95 211°, 64% yield; II (R = furfurylmethyl, R' = 1-C10H7), b2 194-5°, n22D 1.611,71.8%, m. 46.5-8° (EtOHC6H14); II (R = tetrahydrofurfuryl, R' = 1-C10H7), b0.4 154°, 67%; II [R = 2-(tetrahydrofurfuryl)ethyl, R'' = 1-C10H7], b0.4 183°, 60%; II (R = 1-propenyl, R' = 1-C10H7], b0.9 138°, 65.7%; II (R = vinyl, R' = 1-C10H7), b0.4 130°, n19.5D 1.603, d21 1.0520, 85.6%; II (R = HC:C, R' = 1-C10H7), b1 156°, n18D 1.615, m. 63-7° (EtOAc),32%; III (R = H, R' = furfurylmethyl, R'' = 1-C10H7CH2), b1.5 207-9°, m. 72-4° (EtOAc-C6H14), 72%; III (R = Me, R' = furfurylmethyl, R'' = 1-C10H7CH2), b2 193-5°, d25 1.3333, n23D 1.583; III (R = CH2CH2NEt2, R' = furfurylmethyl, R'' = 1-C10H7CH2), b1 188-90°, n21D 1.5728, 60.5%; III [R = H, R' = 3-(tetrahydrofurfuryl)propyl, R'' = 1-C10H7CH2], b1 220-2°, 77%, m. 261° (R = Na, decomposition); III [R = Me, R' = 3-(tetrahydrofurfuryl)propyl, R'' = C10H7CH2], b0.6 178°, d24 1.182, 57.7%; III (R = H, R' = furfuryl, R'' = 1-C10H7), b2 218-19°, m. 80-2° (EtOAc-C6H12), 71.3%, m. 302-3° (Na salt, H2O); III [(CO2R =)CONH2 R' = furfuryl, R'' = 1-C10H7], m. 107-8° (EtOH), 30.2%; III (R = Me, R' = furfuryl, R'' = 1-C10H7), b0.7 158°, d24 1.1375, n23D 1.596, 67%; III (R = CH2CH2NEt2, R' = furfuryl, R'' = 1-C10H7), b1.5 215-16°, n24D 1.5745, 46%; III (R = H, R' = tetrahydrofurfuryl, R'' = C10H7), b1.5 217-18°, m. 135° (EtOAc-C6H14), 66.5%; III [(CO2R =)CONH2, R' = tetrahydrofurfuryl, R'' = 1-C10H7], m. 153-3.5° (EtOAc), 75%; III (R = Me, R' = tetrahydrofurfuryl, R'' = 1-C10H7), b0.36 157-8°, 75.5%; II (R = Et2NCH2, R' = tetrahydrofurfuryl, R'' = 1C10H7), b0.36 191-4°, 51.5%; III [R = H, R = 2-(tetrahydrofurfuryl)ethyl, R'' = 1-C10H7], b0.35 210°, 57.5%; III (R = H, R' = MeCH:CHCH2, R'' = 1-C10H7), b0.7 167° [amide m. 121-2° (EtOAc), 87.7%]; III (R = H, R' = allyl, R'' = 1-C10H7), b0.67 157-8°, 55%.

IT **95432-29-4**, Malonic acid, furfuryl(1-naphthylmethyl)-, diethyl ester
(preparation of)

RN 95432-29-4 CAPLUS

CN Propanedioic acid, (2-furanylmethyl)(1-naphthalenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 69 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1962:475807 CAPLUS
DN 57:75807
OREF 57:15044b-i,15045a-i
TI Substituted aliphatic acids with hypocholesteremie activity
AU Szarvasi, Etienne; Neuvy, Liliane
CS Soc. Lipha, Lyon
SO Bulletin de la Societe Chimique de France (**1962**) 1343-54
CODEN: BSCFAS; ISSN: 0037-8968
DT Journal
LA Unavailable
AB Diethyl furfurylmalonate (140.8 g.) was heated to boiling with 14 g. Na in 400 ml. EtOH, the solution cooled, 72 g. PhCH2Cl added, the mixture refluxed 24 hrs., poured into H2O, worked up through C6H6, and the dried product fractionated to give 5.7 g. liquid, b2.5 53-100°, 4.6 g. liquid, b2 101-59°, and 157 g. R(CH2)nC(CO2Et)2R' (I) (R = 2-furyl, R' = Ph-CH2,n = 1)(II),b2 163-4°, b0.15 138-40°, d23 1.095, n22D 1.511. Similarly were prepared (product, % yield, b.p./mm., d./temperature, and nD/temperature given): I (R = 2-furyl, R' = furfuryl, n = 1) (III), 80, 148-50°/1.5 (134-7°/0.7), 1.118/20°, 1.491/17°; I (R = 2-furyl, R' = tetrahydrofurfuryl, n = 1) (IV), 60, 150-4°/3, -, -; I (R = 2-tetrahydrofuryl, R = PhCH2, n = 3) (V), 80, 176-8°/1, 1.0640/20.5°, 1-505/18°; I (R = 2-furyl, R' = α-naphthylmethyl, n = 1) (VI), 69, 202-3°/1.5, -, -; I (R = 2-tetrahydrofuryl, R' = α-naphthylmethyl, n = 3) (VII), 65, 211° /0.95, -,I (R = 2-tetrahydrofuryI, R' = α-naphthylmethyl, n = 1), 78, 200°/1, -, -. In the condensations involving furfuryl chloride (VIII) and tetrahydrofurfuryl bromide, preparation of III and IV, resp., EtOH was replaced by Et2CO3. II (108.8 g.) was refluxed 15 hrs. with 37.6 g. KOH in 2800 ml. PhCH2OH, the solvent evaporated in vacuo, and the residue dissolved in H2O. The cloudy solution was washed with Et2O, acidified (Congo red) with HCl, extracted with C6H6, the extract dried, the solvent evaporated, and the residue fractionated to give 50 ml. PhCH2OH, a few drops of a liquid, b<1 58-150°, and 65.3 g. R(CH2)nCHR'CO2H (IX) (R = 2-furyl, R' = PhCH2, n = 1) (X), b<1 152-3°, solidified to give crystals, m. 38-40° (unless otherwise stated, m.ps. were determined on a Kofler hot stage); 9.7 g. crude X recrystd. from 30 ml. pentane (refrigerator) and dried in vacuo gave X, m. 40-3° (capillary), b0.8 143-4°; X Na salt (XI) m.

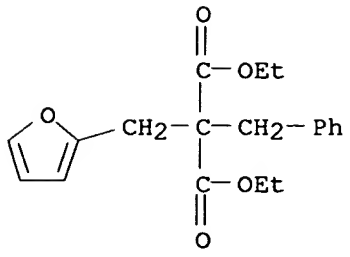
253-4° (capillary). Similarly were prepared (starter, product, % yield, b.p./mm., m.p., and m.p. of salt given): III, IX (R = 2-furyl, R' = furfuryl, n = 1) (XII), 72, 141-3°/1, 56-8° (AcOH), Na salt (XIII) 220-2° (decomposition) (capillary); IV, IX (R = 2-furyl, R' = tetrahydrofurfuryl, n = 1) (XIV), 83, 163-5°/ 1, 79-80° (capillary) (Me2CO), 243° (decomposition) (capillary); V, IX (R = 2-tetrahydrofuryl, R' = PhCH2, n = 3) (XV), 86,178-82°/>1 (n21.5D 1.5225), -, 230° (decomposition) (capillary); VI, IX (R = 2-furyl, R' = α-naphthylmethyl, n - 1) (XVI), 72, 207-9°/1.5, 72-4° (EtOAc-hexane), Na salt (XVII) 260-2° (capillary); VII, IX (R = 2-tetrahydrofuryl, R' = α-naphthylmethyl, n = 3) (XVIII), 81, 220-2°/1, -, Na salt (XIX) 261 (decomposition) (capillary) (hygroscopic). XII (22 g.) in 100 ml. dry C6H6 refluxed 8.5 hrs. with 8.5 g. piperidine (XX) and the C6H6 evaporated gave 26.5 g. crude XII piperidinium salt (XXI), m. 96-8° (capillary) (EtOAc). Similarly, X gave X piperidinium salt (XXII), m. 102-3° (capillary) (EtOAc), in 100% yield. α-Naphthylacetonitrile (196 g.) was refluxed 1 hr. with 58 g. 90% NaNH2 in 580 ml. Et2O, 157 g. VIII in 157 ml. Et2O then added, reflux continued 6 hrs., and the mixture worked up to give 208 g. R(CH2)nCHR'CN (R' = α-naphthyl) (XXIII) (R = 2-furyl, n = 1) (XXIV), b0.5 164-6°, n22D 1.611, m. 46.5-8.0° (EtOH-hexane). Similarly were prepared product, % yield, b.p./mm., and m.p. given): XXIII (R = 2-tetrahydrofuryl, n = 1) (XXV), 67, 184-7°/1 (154°/0.4), 44-6° (EtOH-hexane); XXIII (R = 2-tetrahydrofuryl, n = 3) (XXVI), 69, 182-4°/0.5, -; XXIII (R = MeCH:CH, n = 1) (XXVII), 82, 147-9°/0.4,-; XXIII (R = CH2:CH, n = 1) (XXVIII), 86, 132°/0.5 (d21 1.0520, n19.5D 1.603), -; XXIII (R = CH.tplbond.C, n = 1), 32, 156°/1 (n18D 1.615), 63-7° (EtOH). XXIV (79 g.) refluxed 15 hrs. with 20 g. KOH in 1660 ml. PhCH2OH and worked up as above gave 56.5 g. IX (R' = α-naphthyl) (XXIX) (R = 2-furyl, n = 1) (XXX), b2 218-19°, which solidified when rubbed with a glass rod, m. 84.5-5.5° (EtOAc-hexane); Na salt (XXXI) m. 302-3°. Similarly were prepared (starter, product, % yield, b.p./mm., m.p., and m.p. of salt given): XXV, XXIX (R = 2-tetrahydrofuryl, n = 1) (XXXII), 67, 217-18°/1.5, 135°, Na salt (XXXIII) 250-1° (capillary); XXVI, XXIX (R = 2-tetrahydrofuryl, n = 3) (XXXIV), 75, 210°/0.35, -, Na salt (XXXV) - (hygroscopic); XXVII, XXIX (R = MeCH:CH, n = 1) (XXXVI), 79, 167°/0.7, -, Na salt (XXXVII) - (hygroscopic); XXVIII, XXIX (R = CH2:CH, n = 1), 65, 157-8°/0.6, 84-7° (EtOAc-hexane), Na salt (XXVIII) - (hygroscopic). Neopentyl esters were prepared by azeotropic distillation in C6H6;

other esters were prepared by treatment of the acid with excess boiling alc. Thus were prepared (acid, ester, % yield, b.p./ mm., d./temperature, and nD/temperature given): X, Me (XXXIX), 87.5, 121-2°/1, 1.0783/20°, 1.5265/19°; X,neopentyl, 46, 166°/2, 1.006/23°, 1.5072/20°; X, tert-Bu, 47.5, 122°/ >1, 1.0019/25°, 1.505/24°; XII, Me (XL), 82, 100-2°/1, 1.111/19.5°, 1.515/18°; XII, neopentyl, 70, 114°/1, 1.0290/25°, 1.486/24°; XII, tert-Bu, 45, 116°/>1, 1.021/ 23.5°, 1.484/23°; XIV, Me (XLI), 84.5, 131.5°/2.5, 1.0703/ 22°; XIV, neopentyl, 40, 127°/>1, 1.007/25°, 1.4765/25°; XIV, tert-Bu, 66, 120°/>1, 1.003/24°, 1.4737/23°; XV, Me (XLII), 89, 154-5°/2, 1.023/21°, 1.507/21°; XV, neopentyl, 67, 156°/>1, 0.971/23°, 1.4955/22°; XV, tert-Bu, 44, 163°/2, 0.9839/22°, 1.4958/20°; XVI, Me (XLIII), 74, 193-5°/2,

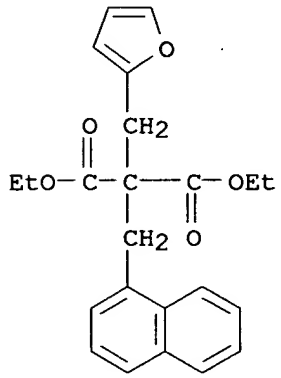
1.1333/25°, 1.583/23°; XVI, tert-Bu (XLIV), 32, 179-80°/2, -, 1.5585/23.5°; XVIII, Me (XLV), 88, 178°/0.6, 1.182/24°, -; XXX, Me (XLVI), 67, 158°/0.7, 1.1375/24°, 1.596/23°; XXX, tert-Bu (XLVII), 49, 171-2°/1, 1.0652/21°, 1.561/21°; XXXII, Me (XLVIII), 76, 157-8°/ 0.36, -, -; XXXII, tert-Bu (XLIX), 59, 182-5°/1,-, 1.551/ 20°; XXXIV, Me (L), 79, 17.9-9.5°/1, -, -; XXXVI, Me (LI), 75, 131-4°/1, 1.0616/22°, 1.5825/22°. XL (32 g.) was refluxed 7 hrs. with 12.2 g. XX and 0.4 ml. AcOH, excess XX removed in vacuo, the cooled residue rubbed with a glass rod, and left overnight in the refrigerator to give 14 g. XXI and 6.5 g. unchanged XL. Similarly, XXXIX gave 63% XXII. XL (40 g.), 21.3 g. HOCH2CH2NH2, 17 ml. PrOH, and 0.4 ml. AcOH were refluxed 16 hrs., the mixture evaporated to dryness in vacuo, the residue left overnight in the refrigerator, stirred with hexane, and filtered to give 40.5 g. N-CH2CH2OH amide of XII, m. 76-7° (EtOAc-hexane then EtOH). XL in iso-PrOH heated with aqueous NH3 gave 38% XII amide, m. 112-13.5° (EtOAc). Similarly were prepared (starter, product, % yield, b.p./mm., and m.p. given): XXXIX, X amide, 28, -, 110-10.5° (EtOAc); XXXIX, N-CH2CH2OH amide of X, 68, 201°/3, 73-4° (EtOAc-hexane); XL, N-CH2CH2CH2OH amide of XII, 95, -, 87-8° (EtOAc); XLI, N-CH2CH2OH amide of XIV, 79, 210-12°/2 (d26 1.1254, n24D 1.514), -; XLII, XV amide, 15, -, 107-8° (EtOAc); XLVI, N-CH2CH2OH amide (LII) of XXX, 88, -, 122-3° (EtOH). XXIV (19.5 g.) was refluxed 50 hrs. with 4.4 g. KOH in 5 ml. H2O and 120 ml. EtOH, the EtOH evaporated, the cooled residue acidified with HCl, and worked up through Et2O to give 105 g. XXX amide (LIII), m. 107-8° (EtOH). Similarly were prepared (starter, product, % yield, and m.p. given): XXV, XXXII amide (LIV), 75, 153-3.5° (EtOAc); XXVI, XXVI amide (LV), 88, 121-2° (sublimed) (EtOAc). XVI - XIX, XXX - XXXVII, and XLIII - LV showed hypocholesteremic activity in the Triton test, XXXI being the most active and having L. D.50 320 and 1250 mg./kg. mouse by intraperitoneal and oral administration, resp. The activity was decreased by saturation of the furan ring or increase in the length of the aliphatic chain, and lost entirely by replacement of the naphthalene system by a benzene ring. Replacement of the furan ring by an unsatd. aliphatic chain strongly decreased hypocholesteremic and hypolipemic activity, e.g. XXXVII, or if hypolipemic activity was largely retained, the hypocholesteremic activity was totally lost, e.g. XXXVIII. XXI and XXII had antiinflammatory activity against the edema produced on the paw of the rat by serotonin, and were 3 and 1.5 times as active, resp., as aspirin. XI and XIII had noteworthy choleretic activity.

IT **94385-69-0**, Malonic acid, benzylfurfuryl-, diethyl ester
95432-29-4, Malonic acid, furfuryl(1-naphthylmethyl)-, diethyl ester
(preparation of)

RN 94385-69-0 CAPLUS
CN Malonic acid, benzylfurfuryl-, diethyl ester (7CI) (CA INDEX NAME)



RN 95432-29-4 CAPLUS
CN Propanedioic acid, (2-furanylmethyl)(1-naphthalenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 70 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1962:462656 CAPLUS
DN 57:62656
OREF 57:12435h-i,12436a-e
TI Aliphatic acids disubstituted by cyclic radicals
IN Szarvasi, Etienne; Neuvy, Liliane
PA LIPHA (Lyonnaise Industrielle Pharmaceutique)
SO 12 pp.
DT Patent
LA Unavailable

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI FR 1278631		19620322	FR	19600729 <--

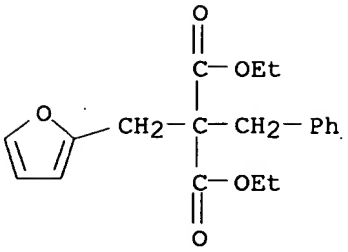
AB The preparation of acids with the general formula R1CH2CH[R2(CH2)n]CHCO2H (n = 1 or 3, R1 = Ph, furyl, or tetrahydrofuryl for n = 1, and Ph for n = 3, R2 = furyl for n = 1, and tetrahydrofuryl for n = 3) and derivs. as esters of primary alcs. with 1-5 C, Na, and piperidine salts, primary and secondary amines, hydrazides, and 2-aminoethanol derivs. is described. These products are of therapeutic value. Thus e.g. 140.8 g. 2-furfurylethyl malonate was added to 400 ml. EtOH containing 14 g. Na and heated to boiling. After cooling, 72 g. PhCH2Cl was added and the mixture refluxed 24 hrs., thrown into H2O, and extracted with C6H6 to give 157 g. Et α-benzyl-α-furylmalonate, b2 163-4°, d234 1.095, n22D 1.511. Similarly described is the preparation of Et α-difurfurylmalonate, b0.7 134-7°, d204 1.118, n17D 1.491; Et

α-furfuryl-α-tetrahydrofurfurylmalonate, b3 150-4°; Et α-benzyl-α-(tetrahydrofurylpropyl)malonate, b1 176-8°, d20.5D 1.0640, n18D 1.505; β-phenyl-β'-furylisobutyric acid, m. 40-3° (Na salt decomposed at 253-4°); β,β'-difurylisobutyric acid, m. 56-8° (AcOH) (Na salt decomposed at 220-2°); β-tetrahydrofuryl-β'-furylisobutyric acid, m. 79-80° (Na salt decomposed at 243°); α-benzyl-δ-tetrahydrofurylvaleric acid, b1 178-82°, n21.5D [Na salt m. 230° (decomposition)]; Me β-phenyl-β'-furylisobutyrate, b. 121-2°, d204 1.0783, n19D 1.5265; isoamyl β-phenyl-β'-furylisobutyrate, b2 166°, d234 1.006, n20D 1.5072; N-diethylaminoethyl β-phenyl-β'-furylisobutyrate, b1 154-5°, d24.54 1.0541, n24.5D 1.525; neopentyl β-phenyl-β'-furylisobutyrate, b1 122°, d254 1.0019, n24D 1.505; methyl β,β'-difurylisobutyrate, b1 100-2°, d19.54 1.111, n18D 1.515; isoamyl β,β'-difurylisobutyrate, b1 114°, d234 1.0290, n24D 1.486; N-diethylaminoethyl β,β'-difurylisobutyrate, b1.5 145.5-8.0°, d23.54 1.0381, n22D 1.493; neopentyl β,β'-difurylisobutyrate, b1 116°, d23.54 1.021, n23D 1.484; methyl β-tetrahydrofuryl-β'-furylisobutyrate, b2.5 131.5°, d224 1.0703, n21D 1.486; isoamyl β-tetrahydrofuryl-β'-furylisobutyrate, b1 127°, d254 1.007, n25D 1.4765; N-diethylaminoethyl β-tetrahydrofuryl-β'-furylisobutyrate, b1 164°, d224 1.0730, n21D 1.4975; neopentyl β-tetrahydrofuryl-β'-furylisobutyrate, b1 120°, d244 1.003, n23D 1.4737; Me α-benzyl-δ-tetrahydrofurylvalerate, b2 154.5°, d214 1.023, n21D 1.507; isoamyl α-benzyl-δ-tetrahydrofurylvalerate, b1, 156°, d234 0.971, n22D 1.4955; N-diethylaminoethyl α-benzyl-γ-tetrahydrofurylvalerate, b1 178°, d214 1.028, n21D 1.5135; neopentyl α-benzyl-δ-tetrahydrofurylvalerate, b2 163°, d224 0.9839, n20D 1.4958; piperidine β-phenyl-β'-furylisobutyrate, m. 102-3°; β-phenyl-β'-furylisobutyramide, m. 109-10° (EtOAc); β-phenyl-β'-furylisobutyrylhydrazine, m. 89-91° (EtOAc); 2-(β-phenyl-β'-furylisobutyramido)ethanol, m. 73-4° (EtOAc-C6H14); piperidine β,β'-difurylisobutyrate, m. 96-8° (EtOAc); β,β'-difurylisobutyramide, m. 112-14° (EtOAc); β,β'-difurylisobutyrylhydrazine, m. 96.5-7.5° (EtOAc); 2-(β,β'-difurylisobutyramido)ethanol, m. 76-7° (EtOH); β-tetrahydrofuryl-β'-furylisobutyrylhydrazine m. 66-8° (EtOAc); 2-(β-tetrahydrofuryl-β'-furylisobutyramido)ethanol, b2 210°, n264 1.1254, n24D 1.514; and α-benzyl-δ-tetrahydrofurylvalerylhydrazine, m. 71.5-2.0° (EtOAc).

IT **94385-69-0**, Malonic acid, benzylfurfuryl-, diethyl ester (preparation of)

RN 94385-69-0 CAPLUS

CN Malonic acid, benzylfurfuryl-, diethyl ester (7CI) (CA INDEX NAME)



L5 ANSWER 71 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1962:73488 CAPLUS
DN 56:73488
OREF 56:14281a-i,14282a-c
TI Pyridylethylbarbituric acids
AU Shapiro, Seymour L.; Bandurco, Victor; Freedman, Louis
CS U.S. Vitamin & Pharm. Corp., Yonkers, NY
SO Journal of Organic Chemistry (**1962**), 27, 174-8
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA Unavailable
OS CASREACT 56:73488
GI For diagram(s), see printed CA Issue.
AB Several 5-pyridylethylbarbituric acids (I), with markedly increased hexobarbital (II) sleeping time, were synthesized. The requisite intermediates were obtained from the corresponding picolyl chloride and the substituted di-Et malonate or by pyridylethylation of the malonate ester. Na (6.6 g.) in 100 ml. alc. refluxed 2.5 hrs. with 26.4 g. EtCH(CO2Et)2 and 22.8 g. 2-C5H4NCH2Cl.HCl, the cooled mixture treated with 100 ml. H2O and 10 ml. HCl, the alc. evaporated, the solution washed with Et2O, treated with 50 ml. 10% aqueous NaOH, extracted with 150 ml. Et2O, and the residue on evaporation of the H2O washed extract distilled yielded 18% product (III). Na (3.0 g.) in 100 ml. alc. refluxed 6 hrs. with 44.0 g. 4-C5H4NCH: CH2, 100 g. EtCH(CO2Et)2, and 0.1 g. hydroquinone, the alc. evaporated, the residue diluted with 200 ml. H2O and 56 ml. HCl, washed with Et2O, treated with 100 ml. 20% aqueous NaOH, the product extracted with Et2O, the extract washed with H2O and aqueous NaHSO3, evaporated, and the residue distilled yielded 65% ester, b0.15 150-60°, hydrolyzed to the malonic acid, m. 146° (MeCN). Similarly were prepared the listed intermediates, C5H4N(CH2)nCR1(CO2Et)2 (position of azine N, n, R1, b.p./mm., and % yield given): 2, 1, Et, 122-8°/0.05, 18; 3, 1, Et, 132°/0.35, 5; 4, 1, Et, 138-42°/0.3, 14; 2, 2, H, 130-4°/0.1, 26; 2, 2, Et, 150-60°/0.15, 65; 2, 2, Et, 150-2°/0.6, 16; 2-(5-EtC5H3N), 2, Et, 160-8°/0.3, 41; 4, 2, H, 140-2°/0.3, 5; 4, 2, Me (IV), 140-50°/0.1, 37; 4, 2, Et, 150-8°/0.45, 50. NaOH (1.8 g.) and 8 g. (4-C5H4NCH2CH2)CPh(CO2Et)2 refluxed 2 hrs. in 20 ml. H2O, the cooled solution diluted with 50 ml. H2O, treated with 4.3 ml. HCl, extracted with warm CHCl3 (50 ml.), and the product recrystd. from dilute alc. yielded 7% 4-C5H4NCH2CH2CHPhCO2H, m. 125-7°. Na (1.0 g.) in 20 ml. alc. treated with 6.0 g. (α-C5H4NCH2)CEt(CO2Et)2 and 1.6 g. (H2N)2CO in

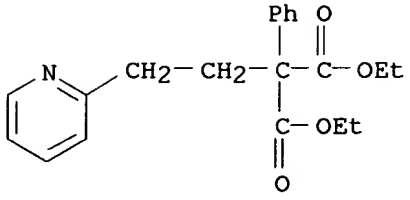
10 ml. hot alc., the mixture refluxed 6 hrs., the cooled solution diluted with 100 ml., the alc. evaporated, and the Et2O-washed residue neutralized yielded 48% I (R = H, R1 = α-C5H4NCH2, R2 = Et), m. 230-2° (BuOH). Similarly were prepared compds. 2 and 3, I (R = H, R1 = β- and γ-C5H4NCH2, R2 = Et), m. 220°, and 234-5°, resp. Na (1.0 g.) in 20 ml. alc., 7 g. (4-C5H4NCH2CH2)CMe (CO2Et)2, and 1.9 g. (H2N)2CS in 20 ml. hot alc. refluxed 9 hrs., the cooled solution diluted with 100 ml. H2O, the alc. evaporated, and the Et2O-washed aqueous residue adjusted to pH 7 yielded 61% compound 21, m. 220-30°. For the 2-imino barbituric acids, an addnl. equivalent of Na alkoxide liberated (H2N)2C:NH from its HCl salt. Employing the appropriately substituted malonate and urea, similarly were prepared the listed compds. 4-35 [series (R1 and R2), number, R, X (if other than O), and m.p./solvent given]. 2-C5H4NCH2CH2, Et: 4, H, 205°/PrOH; 5, H, S, 217-19°/PrOH; 6, H, NH, above 300°/AcOH-MeCN (dipicrate m. 238-40°/alc.); 7, Me, 150-3°/alc.; 8, Et, 123-4°/alc.; 9, H2C:CHCH2, 120°/MeCN; 10, Bu, 85°/alc.; 11, Ph, 185-7°/alc. 2-(5-EtC5H3N)CH2CH2, Et: 12, H, 220-2°/MeCN; 13, H, S, 201-2°/MeCN; 14, H, NH, 280° (decomposition)/AcOH-alc.; 15, Me, 154°/alc.; 16, Et, 137-8°/alc.; 17, H2C:CHCH2, 127-8°/MeCN; 18, Bu, 80-1°/Et2O-C6H14; 19, Ph, 166-7°/alc. 4-C5H4NCH2CH2, Me: 20, H, 252-4°/MeOH; 21, H, S, 227-30°/PrOH; 22, H, NH, over 300°/MeOH; 23, Me, 204-6°/alc.; 24, Et, 176-7°/MeCN; 25, Bu, 174-5°/alc.; 26, Ph, 125-6°/MeOH. 4-C5H4NCH2CH2, Et: 27, H, 224-6°/MeCN; 28, H, S, 224-6°/PrOH; 29, H, NH, above 300°/PrOH (di-HCl salt m. 210-12°/alc.); 31, Me, 148-50°/alc.; 32, Et, 110°/alc.; 33, H2C:CHCH2, 115°/MeCN; 34, Bu, 102-4°/Et2O-C6H14; 35, Ph, 177-8°/alc. No critical stage was noted with pyridylethyl substituents and average yields of 26-29% were noted. As R1 was varied from H, Me, Et, C3H5 Bu, and Ph (X = O), average yields of 20, 24, 41, 14, 30, and 33%, resp., were obtained. Na (1.2 g.) in 50 ml. alc. and 2.6 g. (H2N)2CO in 20 ml. alc. refluxed 7 hrs. with 17.6 g. (2-C5H4NCH2CH2)CPh(CO2Et)2, the cooled mixture diluted with 100 ml. H2O, the alc.-free aqueous residue extracted with 100 ml. Et2O, and neutralized yielded 11% 2-C5H4NCH2CH2CHPhCONH2, m. 121-3° (alc.). The Et2O extract evaporated and the residue crystallized gave 0.5 g. 2-C5H4NCH2CH2CHPhCO2H, 161-2° (alc.). Treatment of 3.9 g. 5-ethylbarbituric acid in 100 ml. alc. with 5.2 g. 4-C6H4NCH:CH2 (exothermic reaction) and recrystn. of the product yielded 40% compound 27, mixed m.p. 224-6°. Similarly, 1 g. 5-phenylbarbituric acid and 0.5 g. 4-C5H4NCH:CH2 in 25 ml. hot 1:1 H2O-alc. evaporated on a steam bath and the precipitate recrystd. from 35 ml. 6:1 H2O-alc. yielded 47% of the otherwise inaccessible I (R = H, R1 = 4-C5H4NCH2CH2, R2 = Ph), compound number 36, m. 248-9°. The effects of structure on the ultraviolet absorption spectra and the pKa were noted, discussed, and the measurements tabulated. The compds. were without substantial toxicity or central nervous system depressant effects. The most conspicuous effect was enhancement of II sleeping time, particularly with compound 31, which showed a 420% increase. The (4-pyridyl)ethyl compds. showed greater effects than the 2-congeners.

IT **94577-33-0**, Malonic acid, phenyl[2-(2-pyridyl)ethyl]-, diethyl ester **94577-34-1**, Malonic acid, phenyl[2-(4-pyridyl)ethyl]-, diethyl ester
(preparation of)

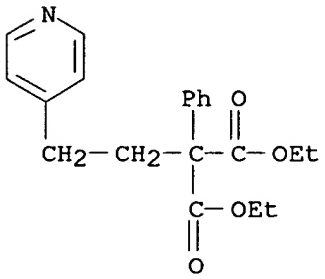
RN 94577-33-0 CAPLUS

CN Malonic acid, phenyl[2-(2-pyridyl)ethyl]-, diethyl ester (7CI) (CA INDEX

NAME)



RN 94577-34-1 CAPLUS
CN Malonic acid, phenyl[2-(4-pyridyl)ethyl]-, diethyl ester (7CI) (CA INDEX NAME)

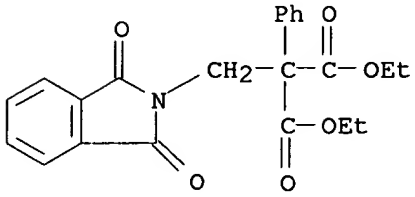


L5 ANSWER 72 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1962:2254 CAPLUS
DN 56:2254
OREF 56:424f-h
TI N-Substituted acid amides
IN Boehme, Horst; Eiden, Fritz
PA Farbwerke Hoechst A.-G.
DT Patent
LA Unavailable

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 1096360		19610105	DE	<--

AB N-Chloromethylimides treated with compds. containing a C with a single H in the presence of cyano, carbalkoxy, carbaryloxy, aldehydo, acetal or acyl groups gave good yields of N-substituted imides. o-C6H4-(CO)2NCH2Cl (I) (1.9 g.) suspended in 10 g. dry Et2O added to NaCMe(CO2Et)2 (II) suspended in 20 g. Et2O yielded under reflux 3 hrs., a slimy precipitate which, washed with Et2O, and freed of Et2O yielded 2.7 g. o-C6H4(CO)2NCHC2Me(CO2Et)2, m. 96° (iso-Am2O). I treated with NaCNHAc(CO2Et)2, NaCEt(CO2Et)2, NaCPh(CN)Ac, NaCMe(CO2Et)Ac, NaCMe(Bz)Ac, and NaCPh(CO2Et)2 yielded, resp. 60% RCMe(CO2Et)2 [R = o-C6H4(CO)2NCH2], m. 138° (dilute alc.); 67% RCEt(CO2Et)2, m. 89° (alc.H2O); 72% RCPh(CN)Ac, m. 139° (alc.); 63% RCMe(CO2Et)Ac, plates, m. 107° (dilute alc.); 54% RCMe(Bz)Ac, m. 169° (alc.); 83% RCPh(CO2Et)2, double pyramids, m. 75-60° (MeOH). ZCH2Cl (Z = o-C6H4.SO2.N.CO) with II, and with NaCMe(CO2Et)CN yielded resp. 59% ZCH2-CMe(CO2Et)2, m. 94° (alc.), and 61% ZCH2CMe(CO2Et)CN, m. 141° (iso-Am2O). (CH2CO)2NCH2Cl with II yielded 47% (CH2CO)2NCH2CMeCO2Et)2, b0.0(110-14°.

IT **112864-34-3**, Malonic acid, phenyl(phthalimidomethyl)-, diethyl ester
(preparation of)
RN 112864-34-3 CAPLUS
CN Propanedioic acid, [(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenyl-, diethyl ester (9CI) (CA INDEX NAME)



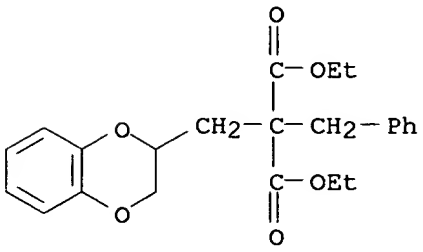
L5 ANSWER 73 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1961:27891 CAPLUS
DN 55:27891
OREF 55:5496d-i
TI Benzodioxan series. XIV. 1,4-Benzodioxan-2-ylmethylmalonic and α-substituted 2-(1,4-benzodioxan)propionic acids
AU Marini-Bettolo, G. B.; Landi-Vittory, Rodolfo; Carvalho-Ferreira, Paulo
CS Ist. superiore sanita, Rome
SO Gazzetta Chimica Italiana (**1959**), 89, 2280-90
CODEN: GCITA9; ISSN: 0016-5603
DT Journal
LA Unavailable
AB cf. CA 54, 1522e. Treatment of 1,4-benzodioxan-2-methyl bromide (QBr) (I), with NaCR(CO2Et)2 according to L.-V. (CA 54, 1523e) gave QCR(CO2Et)2 (II) together with Q2(CO2Et)2 (III). Dry dioxane (15 ml.) containing 0.1 mole I refluxed (N atmospheric) and stirred with dropwise addition of NaCR(CO2Et)2 (0.1 mole Na and 0.13 mole RCH(CO2Et)2 in 20 ml. dry dioxane), the mixture refluxed 20 hrs. with stirring, the dioxane evaporated, the residue treated with H2O, extracted with Et2O, and the product distilled gave II (R, b.p./mm., and nD/temperature given): H, 140-50°/0.1, 1.5035/20°; Me, 114-15°/0.001, 1.4952/22°; Et, 140-50°/0.1, 1.4950/23°; Pr, 135-40°/0.03, 1.4921/22°; Me2CH, 148-56°/0.12, 1.4969/26°; Bu, 150-5°/0.1, -; Ph, 178-80°/0.2, 65-70°, -; PhCH2, 170-85°/0.02, 1.5299/22°. I treated with NaCH(CO2Et)2 gave by-product III, b0.1 210°, m. 105-10°, also produced directly from I and Na2C(CO2Et)2. II (0.1 mole) refluxed 4 hrs. in 150 ml. 8% aqueous NaOH and 30 ml. alc., the cooled mixture acidified with dilute HCl, the oily product shaken with CHCl3, extracted with dilute aqueous Na2CO3, acidified, and the product recrystd. from H2O, or organic solvents gave QCR(CO2H)2 (IV) (R and m.p. given): Me, 164° (H2O) [λ 278, 284 mμ (log ε 3.42; 3.37)]; Et, 187° (alc.); Bu, 160° (C6H6); PhCH2, 168° (C6H6-Me2CO). On heating above the m.p., IV gave the corresponding substituted propionic acid, QCHRCO2H (V), also obtained by partial decarboxylation by acidification in the preparation of IV. II (0.1 mole) in 200 ml. 1:6:3 H2O-AcOH-H2SO4 refluxed 10-12 hrs., diluted with 500 ml. H2O, stirred with CHCl3, and the H2O-washed CHCl3 extracted with 8% aqueous NaOH, acidified with dilute HCl, and the oily slowly-solidifying product

recrystd. from H2O or organic solvents gave V [R and m.p. (solvent) or b.p./mm. given]: Me, 125° (MeOH) [λ 278, 284 mμ (log ε 3.36, 3.31)]; Et, 155-62°/0.6; Bu, 130-40°/0.03; Ph, 146° (MeOH) [λ 278, 284 mμ (log ε 3.49, 3.44)]; PhCH2, 160-5°/0.03; H, 150° (H2O). V (R = Ph) obtained by acid or alkaline hydrolysis gave a mixture, which yielded a readily crystallizing form, m. 146° (MeOH), and a difficultly crystallizing isomer, m. 100° (dilute alc.), soluble in alkali and transformed by heating in H2O to the more stable isomer. Both forms showed the same infrared spectrum in CCl4 but presented some differences in Nujol. V provide suitable intermediates for synthesis of N derivs. in the benzodioxan series.

IT **114842-77-2**, Malonic acid, (1,4-benzodioxan-2-ylmethyl)benzyl-, diethyl ester **116154-39-3**, Malonic acid, (1,4-benzodioxan-2-ylmethyl)phenyl-, diethyl ester
(preparation of)

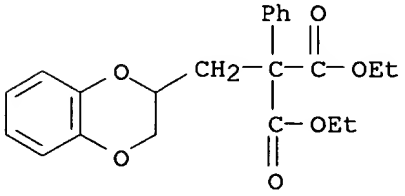
RN 114842-77-2 CAPLUS

CN Malonic acid, (1,4-benzodioxan-2-ylmethyl)benzyl-, diethyl ester (6CI) (CA INDEX NAME)



RN 116154-39-3 CAPLUS

CN Malonic acid, (1,4-benzodioxan-2-ylmethyl)phenyl-, diethyl ester (6CI) (CA INDEX NAME)



L5 ANSWER 74 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1959:121796 CAPLUS

DN 53:121796

OREF 53:21795d-i,21796a

TI Amidomethylations of CH-acidic compounds with diacylimidochloromethanes

AU Bohme, Horst; Broese, Reinhold; Eiden, Fritz

CS Univ. Marburg, Germany

SO Chemische Berichte (**1959**), 92, 1258-62
CODEN: CHBEAM; ISSN: 0009-2940

DT Journal

LA Unavailable

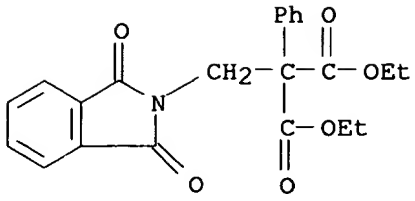
OS CASREACT 53:121796

AB β-Dioxo compds. which are substituted in the methylene group can be amidomethylated by reaction with diacylimidochloromethanes. Phthalimidomethanol (1.8 g.) and 2.1 g. PCl5 each in 10-15 cc. dry Et2O mixed, shaken, heated 10 min. on the water bath, cooled with ice-NaCl, diluted with shaking with iced H2O, and filtered yielded 1.6 g. phthalimidochloromethane (I), m. 134-5° (CCl4). I (19.5 g.) in 30 cc. Et2O added to 19.0 g. EtCH(CO2Et)2 and 2.3 g. Na in 150 cc. dry Et2O, heated 2 h. on the water bath, cooled, and diluted with H2O, the Et2O layer worked up, and the residue washed with petr. ether yielded 23.0 g. di-Et ethyl(phthalimidomethyl)malonate (II), m. 89° (EtOH). II (4.0 g.) and 50 cc. fuming HCl heated 2 h. in a sealed tube at 170°, cooled, filtered, and evaporated in vacuo yielded 1.5 g. H2NCH2CHEtCO2H.HCl, m. 119° (EtOH-Et2O). Na (1.4 g.) in 30 cc. absolute EtOH refluxed 6 h. with 7.0 g. II and 1.8 g. urea, cooled, concentrated on the water bath, dissolved in H2O, and treated with HCl gave 3.5 g. 5-phthalimidomethyl-5-ethylbarbituric acid, leaflets, m. 249-51° (hot H2O). AcMeCHCO2Et (14.4 g.), 2.3 g. Na, and 19.5 g. I gave in the usual manner 19.0 g. di-Et methyl(phthalimidomethyl)acetoacetate, m. 107° (dilute EtOH). I (19.5 g.) and 18.1 g. [AcPhCCN]Na refluxed in dry Me2CO, cooled, and poured into H2O yielded 23.0 g. phenyl(phthalimidomethyl)acetoacetonitrile (III), m. 139° (EtOH). A similar run in absolute EtOH yielded 22.0 g. phenyl(phthalimidomethyl)acetonitrile (IV), m. 124° (MeOH). IV heated 2 h. with fuming HCl yielded 86% H2NCH2CHPhCO2H.HCl, m. 201° (EtOH-Et2O). BzMeCHAc (17.6 g.) treated with 2.3 g. Na, the product suspended in dry Me2CO, the suspension refluxed 0.5 h. with 19.5 g. I, cooled, and poured into H2O gave 18.0 g. 1-methyl-1-phthalimidomethyl-1-benzoylacetone, m. 169° (EtOH or Me2CO). The Na salt from 7.7 g. 1,1,4-trimethyl-3,5-cyclohexanedione (V) and 9.9 g. I heated 0.5 h. in absolute EtOH on the water bath and poured into H2O yielded 15.0 g. 4-phthalimidomethyl derivative of V, m. 159° (EtOH). Ph2CHCHO (2.1 g.), 0.4 g. NaH, and 50 cc. dry Et2O refluxed several hrs. with stirring, the supernatant decanted and treated with 2.0 g. I in 20 cc. dry Et2O, the mixture heated 10 min. with stirring, and the Et2O evaporated gave phthalimidomethyldiphenylacetaldehyde (VI), m. 99° (EtOH). VI gave with NH2OH solution the oxime, m. 130° (EtOH). MeCH(CO2Et)2 (23.6 g.) and 3.1 g. in 50 cc. dioxane added at room temperature with stirring to 20.0 g. succinimidochloromethane in 50 cc. dioxane, the dioxane evaporated in vacuo, the residue dissolved in Et2O, and the solution washed, dried, and distilled gave 18.0 g. di-Et methyl(succinimidomethyl)malonate, viscous oil, b0.01 110-14°. By the method described for the preparation of II were obtained the following compds. (m.p., % yield, and reaction medium given): di-Et methyl(phthalimidomethyl)malonate (VII), 96° (iso-Am2O), 81, Et2O; di-Et phenyl(phthalimidomethyl)malonate (VIII), 75-6° (MeOH), 83, Et2O; di-Et acetamido(phthalimidomethyl)malonate (IX), 138° (aqueous EtOH), 60, absolute EtOH. VII heated with concentrated HCl and decarboxylated gave H2NCH2CHMeCO2H.HCl, m. 128-9° (EtOH-Et2O). VIII yielded similarly H2NCH2CHPhCO2H.HCl, m. 201° (EtOH-Et2O), and IX gave in the same manner H2NCH2CH(NH2)CO2H.HCl, m. 225° (aqueous EtOH).

IT **112864-34-3**, Malonic acid, phenyl(phthalimidomethyl)-, diethyl ester
(preparation of)

RN 112864-34-3 CAPLUS

CN Propanedioic acid, [(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenyl-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 75 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1959:51232 CAPLUS
DN 53:51232
OREF 53:9258f-h
TI Halopyrazines
IN Druey, Jean; Huni, Albrecht; Ringier, Beat H.; Staehelin, Alex
PA C I B A Ltd.
DT Patent
LA Unavailable
FAN.CNT 1

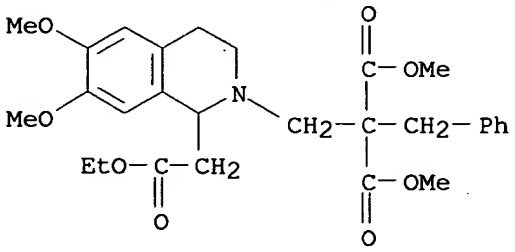
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 325291		19571214	CH	<--

AB Title compds. are valuable antipyretics and are intermediates in the preparation of the medicinally useful 5,6-diamino-2-aryl-3-oxodihydropyridazines. The reaction of 5,6-dihalo-3-oxo-2,3-dihydropyridazines, having a substituted or unsubstituted aryl group in position 2 (C.A. 52, 458i), with ammonia or amines yields 5-amino-6-halo-2-aryl-3-oxo-2,3-dihydropyridazines. Thus, 14.25 g. 5,6-dichloro-2-phenyl-3-oxo-2,3-dihydropyridazine (I), m. 138°, 200 cc. EtOH, and 9 cc. morpholine refluxed 4 h. gave 6-chloro-5-morpholino-2-phenyl-3-oxo-2,3-dihydropyridazine, m. 168-9° (EtOH). I (16 g.), 200 cc. EtOH, and 12 g. piperidine refluxed 5 h. gave 6-chloro-5-piperidino-2-phenyl-3-oxo-2,3-dihydropyridazine, m. 118.5-19.5° (EtOH). I (6.4 g.) heated with 20 cc. 30% alc. Me2NH solution 6 h. in a sealed tube gave 6-chloro-5-dimethylamino-2-phenyl-3-oxo-2,3-dihydropyridazine, m. 125-7° (2:1 C6H6-iso-Pr2O).

IT **117866-98-5**, Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolyl]methyl]-, 1-ethyl di-Me ester (preparation of)

RN 117866-98-5 CAPLUS

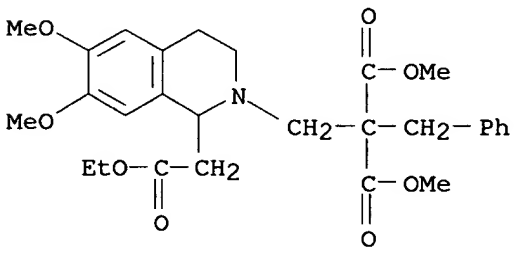
CN Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)isoquinolyl]methyl]-, 1-ethyl dimethyl ester (6CI) (CA INDEX NAME)



L5 ANSWER 76 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1959:51231 CAPLUS
DN 53:51231
OREF 53:9258f
TI Diquaternary compounds
IN Billinghurst, John E. W.
PA Wellcome Foundation Ltd.
DT Patent
LA Unavailable
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 802870		19581015	GB	<--

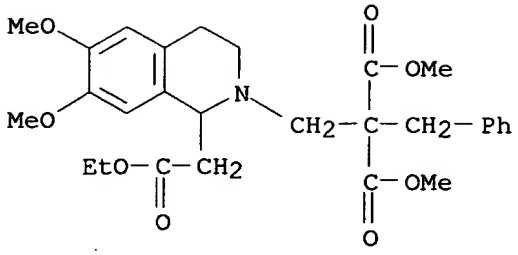
AB See U.S. 2,851,459 (C.A. 53, 5294g).
IT **117866-98-5**, Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolyl]methyl]-, 1-ethyl di-Me ester (preparation of)
RN 117866-98-5 CAPLUS
CN Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)isoquinolyl]methyl]-, 1-ethyl dimethyl ester (6CI) (CA INDEX NAME)



L5 ANSWER 77 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1959:51230 CAPLUS
DN 53:51230
OREF 53:9258e-f
TI 2-Oxobenzo[a]quinolizines
IN Brossi, Arnold; Schnider, Otto; Walter, Max
PA Hoffmann-La Roche Inc.
DT Patent
LA Unavailable
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2830993		19580415	US	<--

AB See Brit. 789,789 (C.A. 53, 4316e).
IT **117866-98-5**, Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolyl]methyl]-, 1-ethyl di-Me ester (preparation of)
RN 117866-98-5 CAPLUS
CN Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)isoquinolyl]methyl]-, 1-ethyl dimethyl ester (6CI) (CA INDEX NAME)



L5 ANSWER 78 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1959:23433 CAPLUS
DN 53:23433
OREF 53:4316d-i
TI 2-Oxobenzo[a]quinolizines
PA F. Hoffmann-La Roche & Co. Akt.-Ges
DT Patent
LA Unavailable
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI GB 789789		19580129	GB		<--

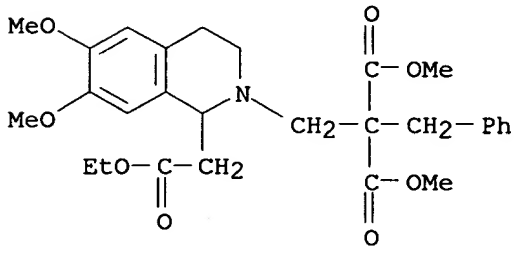
AB 1-(Alkoxycarbonylmethyl)-1,2,3,4-tetrahydroisoquinoline or the 1,2,3,4,5,6,7,8-octahydro analog, both of which may contain lower (not more than 3 C) alkoxy or an alkylenedioxy group at the 6 and 7 positions is condensed with formaldehyde or paraformaldehyde and malonic acid or its dimethyl ester which contains an alkyl or aralkyl group of not more than 8 C or the tetrahydrofurfuryl group. The resulting product is cyclized by heating with an alkaline condensing agent, then hydrolyzed and decarboxylated. The salt of the 2-oxo-3-substituted-1,2,3,4,6,7-hexahydrobenzo[a]quinolizine or its derivative in which the benzo moiety is partially hydrogenated and (or) contains lower alkoxy or alkylenedioxy substituents at the 9 and 10 positions is converted to its free base or salts. Thus, 1-ethoxycarbonylmethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (280 g.), 35 g. paraformaldehyde, and 150 g. CH2(CO2Me)2 were heated under reflux in 1000 ml. MeOH. On cooling 1-ethoxycarbonylmethyl-2-[2,2-bis(methoxycarbonyl)propyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (I), m. 89-91°, crystallized Na (28 g.) was dissolved in 500 ml. MeOH, the solution evaporated to dryness, 3500 ml. toluene and 440 g. I added, and the mixture heated with stirring. After the MeOH had distilled and the b.p. of toluene was reached, the mixture was refluxed 2 hrs. and evaporated to dryness. The residue was heated under reflux for 16 hrs., cooled, and made alkaline with NH4OH to precipitate 2-oxo-3-methyl-9,10-dimethoxy-1,2,3,4,6,7-hexahydrobenzo [a]-quinolizine (II), m. 138-40°; HCl salt, m. 204-5°. Also prepared by similar procedures were 2-oxo-3-R-substituted-9,-10 - dimethoxy - 1,2,3,4,6,7 - hexahydrobenzo[a]quinolizines (R, and m.ps. base, HCl salt, and HBr salt given); Me, 138-40°, 204-5°, -; Et, 110-20°, 198-200°, 218°; iso-Pr, 123-4°, -, 222-3°; allyl, 116-17°, -, 204-5°; Bu, 112-14°, 188-9°, -; benzyl, 139-41°, 165-7°, -; iso-Bu, 126-8°, 196-7°, -; Am, 121-2°, 184-5°, -; hexyl, 92-4°, 173-5°, -. Also prepared similarly were 2-oxo-3-ethyl-1,2,3,4,6,7,8,9,10,11-decahydrobenzo[a]quinolizine, m. 69° (HCl salt, m. 122°);

2-oxo-3-ethyl-9,10-methylenedioxybenzo-[a]quinolizine, m. 147-9° (HCl salt, m. 187-9°); 2-oxo-3-ethyl-9,10-diethoxybenzo[a]quinolizine, m. 116-18°; 2-oxo-3-tetrahydrofurfuryl-9,10-dimethoxybenzo[a]quinolizine, m. 102-4° (HBr salt, m. 194-5°).

IT **117866-98-5**, Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolyl]methyl]-, 1-ethyl di-Me ester (preparation of)

RN 117866-98-5 CAPLUS

CN Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)isoquinolyl]methyl]-, 1-ethyl dimethyl ester (6CI) (CA INDEX NAME)



L5 ANSWER 79 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1956:8410 CAPLUS

DN 50:8410

OREF 50:1705b-i,1706a-i,1707a-d

TI Podophyllotoxin and picropodophyllin. II. The synthesis of an open-chain analog

AU Drake, Nathan L.; Tuemmler, William B.

CS Univ. of Maryland, College Park

SO Journal of the American Chemical Society (**1955**), 77, 1204-9
CODEN: JACSAT; ISSN: 0002-7863

DT Journal

LA Unavailable

AB cf. C.A. 45, 6616g. The synthesis of α-(3,4,5-trimethoxybenzyl)-β-(α-hydroxy-3,4-methylenedioxybenzyl)butyrolactone (I), an open-chain analog of podophyllotoxin, is described. In addition, the stripped, open-chain analog, α-benzyl-β-(α-hydroxybenzyl)butyrolactone (II) is reported. 3,4,5-(MeO)3C6H2CO2H (III) esterified with EtOH and p-MeC6H4SO3H as the catalyst gave 95% Et ester (IV), m. 52.5-4.5° (all m.ps. are corrected). IV (24.0 g.) in 50 cc. THF added during 20 min. to 50 cc. 2.1M LiAlH4 in THF under N, the mixture refluxed gently 2 h., cooled, treated cautiously with H2O and then 10% H2SO4, the aqueous layer extracted with Et2O, and the combined organic layer and Et2O extract washed with 5% aqueous NaHCO3, dried, and distilled yielded 15.6 g. 3,4,O-(MeO)3C6H2CH2OH (V), viscous oil, b0.03 115-20°. III (25.2 g.) and 5.0 g. LiAlH4 refluxed 21 h. in 185 cc. THF, and the mixture worked up in the usual manner yielded 13.7 g. V, b0.02 115-20°, nD25 1.5431. V (15.6 g.) and 9.7 g. PhNMe2 in 100 cc. dry C6H6 slowly treated with 9.4 g. pure SOCl2 in 25 cc. C6H6, the mixture warmed to room temperature, refluxed 1 h., cooled, and treated with 30 cc. 1:5 HCl, the organic layer freed of acid and concentrated, and the residue distilled yielded 15.0 g. 3,4,5-(MeO)3C6H2CH2Cl (VI), b0.1 110°, m. 58-61°; the distillate recrystd. from petr. ether gave 12.9 g. white crystals, m.

60-2°. NaH (15.4 g.) in 550 cc. CH2(CO2Et)2 treated during 1 h. with 131 g. VI in 350 cc. CH2(CO2Et)2, the mixture heated 20 h. at 105-10°, cooled, treated with a few drops AcOH and 50 cc. H2O, the amber solution decanted from the coagulated salt, the excess CH2(CO2Et)2 removed, and the residue recrystd. from 2.5 l. petr. ether yielded 172.5 g. 3,4,5-(MeO)3C6H2CH2CH(CO2Et)2 (VII), white needles, m. 78-9°. 3,4,5-(MeO)3C6H2CHO (VIII) (0.75 g.), m. 73.8-5.0°, 0.63 g. CH2(CO2Et)2, 0.45 g. AmCO2H, and 0.15 g. piperidine in 35 cc. C6H6 refluxed under a Dean-Stark trap, the solution washed with H2O and 5% aqueous NaHCO3 and evaporated, and the residue recrystd. from 25 cc. petr. ether yielded 0.95 g. 3,4,5-(MeO)3C6H2CH:C(CO2Et)2 (IX), m. 69.2-70.4° (from petr. ether). Approx. 50% of a sample of IX which had stood 20 mo at room temperature no longer dissolved in boiling petr. ether; this material recrystd. from C6H6-petr. ether gave a dimer, m. 212-13°, probably 1,3-bis-(3,4,5-trimethoxyphenyl)-2,2,4,4-tetracarbethoxycyclobutane. IX hydrogenated over PtO2 gave VII. VI (155 g.) gave by the method of Walker and Hauser (C.A. 40, 5712.1) with EtOMgCH(CO2Et)2 217 g. 3,4,5-(MeO)3C6H2COCH(CO2Et)2 (X), white solid, m. 90.5-1.5° (from 1.2 l. 50% aqueous EtOH). X (4.5 g.) and 2.0 g. 10% Pd-C in 100 cc. absolute EtOH hydrogenated at room temperature and 2.5 atmospheric and the crude product recrystd. from 50 cc. petr. ether gave 2.4 g. VIII, m. 73.4-4.0°. X hydrogenated over PtO2 gave 59% CH2(CO2Et)2 and 68% V. V (1.0 g.) in 20 cc. 10% H2SO4 boiled 3 h., the mixture extracted with Et2O, the extract filtered and evaporated slowly, and the small amount crystalline residue recrystd. from EtOH yielded 20 mg. 1,2,3,5,6,7-hexamethoxy-9,10-dihydroanthracene, m. 201.5-203°. 3,4-CH2O2C6H3CO2H (XI) (113.5 g.), m. 230-2°, and 123 cc. pure SOCl2 refluxed 5 h., the excess SOCl2 removed, and the residue distilled gave 124 g. 3,4-CH2O2C6H3COCl (XII), b0.02 92°, m. 78-83°. When XII was prepared by the method of Bruchhausen and Gerhard (C.A. 33, 5391.4) with C6H6 as a diluent a considerable amount of anhydride of XI, m. 152.6-4.2°, was obtained, which boiled with 107% NaOH was hydrolyzed to XI, m. 231-3°. EtOMgCH(CO2Et)2 (XIII) (0.85 mol) in Et2O refluxed 0.5 h. with 139 g. XII in 1 l. Et2O, the mixture cooled, acidified with 10% H2SO4, and allowed to stand overnight, and the resulting deposit of large white crystals recrystd. from EtOAc-petr. ether gave 3,4-CH2O2C6H3COCH(CO2Et)2 (XIV), m. 69.5-71.0°. The crude XIV obtained by the evaporation of the Et2O solution boiled 5 h. with 210 cc. AcOH, 140 cc. H2O, and 27 cc. H2SO4, the orange-red solution made alkaline with 40% aqueous NaOH and extracted with Et2O, the extract washed, dried, and evaporated, and the residue recrystd. from 3 l. petr. ether gave 97 g. 3,4-CH2O2C6H3Ac (XV), pale yellow solid, m. 84-7°; the aqueous solution acidified yielded 6.4 g. XI, m. 230°. XV (49.2 g.) in 1.5 l. dry Et2O treated with 48 g. Br during 40 min., the Et2O evaporated in vacuo, the brick-red residue treated with 500 cc. H2O, washed with more H2O, and recrystd. from 4 l. petr. ether with C gave 56 g. α-Br derivative (XVI), white plates, m. 90-2.5°. XIII (0.11 mol) in Et2O treated with 19.9 g. BzCH2Br in dry Et2O, the mixture refluxed 1.5 h., cooled, and acidified with 75 cc. 10% H2SO4, the Et2O solution evaporated, and the residual oil allowed to stand deposited 3 g. BzCH2CH(CO2Et)2 (XVII), m. 120-1.2°; distillation of the remaining oil gave 8.2 g. CH2(CO2Et)2, 3.1 g. BzCH2Br, and 9.1 g. XVII. Mg (2.43 g.), 2.5 cc. absolute EtOH, and 0.25 cc. CCl4 treated with 25.0 g. PhCH2CH(CO2Et)2, b0.03 100°, nD22 1.4862, in 10 cc. absolute EtOH, the

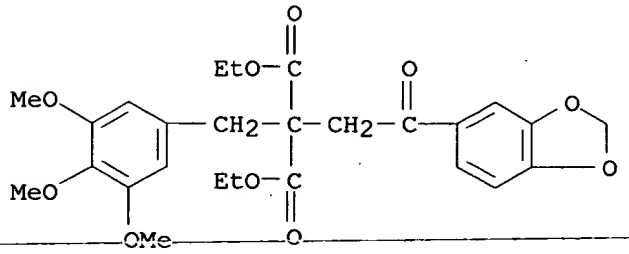
mixture refluxed 1.5 h., the clear solution treated with 150 cc. dry C6H6, the excess EtOH removed as an azeotrope with C6H6, the residual mixture treated with 19.9 g. BzCH2Br in 125 cc. C6H6, the amber solution allowed to stand 7 days at room temperature and acidified with 75 cc. 10% H2SO4, the C6H6 layer evaporated, and the residue recrystd. from 400 cc. petr. ether gave 29.8 g. BzCH2(PhCH2)C(CO2Et)2 (XVIIa), white crystals, m. 75-7°.
3,4,5-(MeO)3C6H2CH2(EtOMg)C(CO2Et)2 (0.23 mol) in C6H6 (prepared from VII) treated with 56 g. XVI in 1 l. C6H6, the mixture kept 7 days at room temperature,
the yellow-green solution acidified with 100 cc. 10% H2SO4, washed with base, and evaporated, and the residue recrystd. twice from 50% aqueous EtOH yielded 88
g. di-Et ester (XVIII), white, m. 104-5°, of 3,4,5-(MeO)3C6H2CH2(3,4-CH2O2C6H3COCH2)C(CO2H)2 (XIX), 2,4-dinitrophenylhydrazone, m. 172.5-4.0°. XVIII (1.0 g.) in 50 cc. EtOH hydrogenated at room temperature and atmospheric pressure over 1.0 g. 10% Pd-C and
the resulting crude product recrystd. twice from EtOH gave 0.3 g. α-CO2Et derivative (XX) of α-(3,4,5-trimethoxybenzyl)-γ-(3,4-methylenedioxyphenyl)butyrolactone (XXI), m. 149.5-51.0°. XVIIa (56.8 g.) in 150 cc. warm absolute EtOH added to 200 g. KOH in 600 cc. absolute EtOH, the mixture cooled, the deposit washed with small portions cold absolute EtOH and then dry Et2O, and dissolved in 400 cc. H2O, and the solution acidified with HCl yielded PhCH2C(CH2Bz)(CO2H)2 (XXII), m. 168-70°.
XVIII (33.8 g.) in 200 cc. warm absolute EtOH added to 175 g. KOH in 600 cc. absolute EtOH, the mixture kept 0.5 h. at room temperature, chilled, and filtered, the
filter residue washed with EtOH and Et2O and dissolved in H2O, and the solution acidified gave XIX.2H2O, m. 132-3° (decomposition) (from EtOAc-petr. ether). Crude moist XXII from 56.8 g. XVIIa decarboxylated thermally and the residue recrystd. from 400 cc. AcOH and 250 cc. H2O yielded 35 g. PhCH2CH(CH2Bz)CO2H (XXIII), m. 173-4.5°; Me ester, 82%, m. 68.2-9.0°. Crude moist XIX.2H2O thermally decomposed at 150° and the resulting yellow glass crystallized from EtOAc-petr. ether with C yielded 22.8 g. 3,4,5-(MeO)3C6H2CH2(3,4-CH2O2C6H3COCH2)CHCO2H (XXIV), m. 133.8-5.4°. XXIV dissolved in MeOH containing dry HCl yielded 68% Me ester, m. 91-2.5° (from EtOAc-petr. ether). XXIV in EtOH containing dry HCl kept 18 h. at room temperature gave the Et ester, m. 117-18° (from EtOH); 2,4-dinitrophenylhydrazone, m. 144-5° (from EtOH). XXIV (3.1 g.) treated 24 h. at room temperature with 1.0 g. NaBH4,
the mixture acidified and extracted with Et2O, the extract reextd. with aqueous NaHCO3,
and the solid from the NaHCO3-extract (after treatment with EtOH) recrystd. twice from aqueous EtOH gave 0.9 g. XXI, m. 95.5-7.5°. XXIII (7.12 g.) in 31.7 cc. 0.926N NaOH treated with 2.40 cc. 37% aqueous CH2O, the mixture kept
48 h. at room temperature and acidified with dilute HCl, the precipitated gum dissolved
in C6H6 and chromatographed on silicic acid, the column eluted with C6H6, the resulting noncryst. product seeded and triturated with C6H6-petr. ether, and the granular residue recrystd. from C6H6-petr. ether yielded 2.40 g. α-benzyl-β-benzoylbutyrolactone (XXV), white solid, m. 108-10°; 2,4-dinitrophenylhydrazone, m. 197-9°. In a similar run with 12 equivs. CH2O chromatog. on silicic acid yielded approx. equal amts. XXV and 3-benzoyl-4-benzyl-4-hydroxy-3-hydroxymethyl-γ,-butyrolactone (XXVI) (which did not form a dinitrophenylhydrazone). XXIV (16.1 g.) in 48 cc. 0.926N NaOH kept 44 h.

at room temperature with 4.5 cc. 37% aqueous CH2O, the mixture chilled and acidified,
the gummy precipitate washed with H2O and triturated several times with Et2O, and
the product (10.9 g.) recrystd. from EtOAc-petr. ether gave pure γ-HO derivative (XXVII) of α-(3,4,5-trimethoxybenzyl)-β-(3,4-methylenedioxybenzoyl)butyric acid (XXVIII), m. 135-7° (decomposition). XXVII heated at 150° until the sample was completely melted and the glassy product crystallized from EtOH gave the lactone of XXVII, m. 140.4-3.0°. XXVII lactone treated in warm EtOH with excess 0.1N NaOH, the mixture kept 0.5 h. at room temperature and back-titrated gave the saponification equivalent; if the mixture was boiled variable, low values were obtained
depending upon the duration of the boiling. The lactone gave a yellow precipitate with 2,4-(O2N)2C6H3NHNH2, but the product did not have a sharp m.p.
XXV (2.38 g.) in 50 cc. EtOH hydrogenated 20 min. at room temperature and atmospheric
pressure over 0.5 g. 10% Pd-C, the mixture filtered and evaporated, and the white solid residue (1.18 g.) recrystd. from 5 cc. EtOH gave 1.01 g. II, m. 149-60° (from C6H6-petr. ether); it was also prepared by the Pd-catalyzed hydrogenation of XXV in cyclohexane. XXV (3.9 g.) (noncryst. material) in EtOH hydrogenated 6 h. over Pd-C yielded 1.11 g. isomer of II, m. 103-3.6° (from C6H6-petr. ether). XXVII lactone (4.14 g.) hydrogenated 3.5 h. in 50 cc. EtOH over 1.3 g. 10% Pd-C the glassy product (3.5 g.) in 45 cc. EtOAc and 60 cc. petr. ether seeded and kept several days at -20° yielded 2.53 g. white powder which recrystd. twice gave 1.87 g. I, m. 104-8°. The noncryst. fraction from the reaction of IV with CH2O yielded about 13% XXVIII, m. 166-7°.

IT **7400-87-5**, Malonic acid, (3,4-methylenedioxyphenacyl)(3,4,5-trimethoxybenzyl)-, diethyl ester
(preparation of)

RN 7400-87-5 CAPLUS

CN Malonic acid, [3,4-(methylenedioxy)phenacyl](3,4,5-trimethoxybenzyl)-, diethyl ester (8CI) (CA INDEX NAME)



=> s l4 not l5
L6 17 L4 NOT L5

=> dis l6 bib abs

L6 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:547244 CAPLUS
DN 141:225396
TI Novel nucleophilic C-C bond-forming tele-reaction of imidazole ring

AU Ohta, Shunsaku; Sato, Kentaro; Kawasaki, Ikuo; Yamaguchi, Yuko; Nishio, Satoko; Yamashita, Masayuki
CS Kyoto Pharmaceutical University, Kyoto, 607-8414, Japan
SO Journal of Heterocyclic Chemistry (2004), 41(3), 335-341
CODEN: JHTCAD; ISSN: 0022-152X
PB HeteroCorporation
DT Journal
LA English
OS CASREACT 141:225396
AB Reaction of 2-(1-chloro-2,2-dimethylpropyl)-1-methyl-1H-imidazole with di-Et methylmalonate in the presence of NaH gave a normal SN product, 2-[(1,1-diethoxycarbonylethyl)-2,2-dimethylpropyl]-1-methyl-1H-imidazole and two tele-reaction products, 5-(1,1-diethoxycarbonylethyl)-1-methyl-2-(2,2-dimethylpropyl)-1H-imidazole and trans-4,5-di-(1,1-diethoxycarbonylethyl)-4,5-dihydro-1-methyl-2-(2,2-dimethylpropyl)-1H-imidazole in 5, 17 and 70 % yields, resp. The scope and mechanism of this reaction are discussed.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> dis l6 2-17 bib abs

L6 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:389622 CAPLUS
DN 140:400059
TI Composition containing activators of IC potassium channels and calcineurin antagonists and their use for the treatment of inflammatory diseases
IN Kaesler, Susanne; Koegel, Heidi; Alzheimer, Christian; Sych, Michael
PA Switch Biotech A.-G., Germany; Ludwig-Maximilians-Universitat; ETH Zurich
SO Ger. Offen., 73 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 10250870	A1	20040513	DE 2002-10250870	20021031
WO 2004039409	A2	20040513	WO 2003-EP12130	20031031
WO 2004039409	A3	20040910		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI DE 2002-10250870 A 20021031
OS MARPAT 140:400059
AB The invention discloses compns., containing activators of IC (intermediate conductance) potassium channels and calcineurin antagonists, as well as their use for the treatment of inflammatory diseases, in particular inflammatory skin diseases.

L6 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

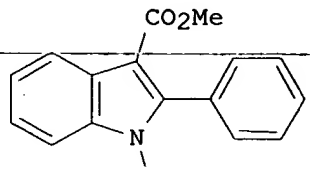
AN 2004:356066 CAPLUS
DN 141:71518
TI Synthesis of original benzo[g]quinoxaline-5,10-diones by bis-SRN1 methodology
AU Remusat, Vincent; Terme, Thierry; Gellis, Armand; Rathelot, Pascal; Vanelle, Patrice
CS Laboratoire de Chimie Organique Pharmaceutique LCOP, UMR CNRS 6517, Faculte de Pharmacie, Universite de la Mediterranee, Marseille, 13385, Fr.
SO Journal of Heterocyclic Chemistry (2004), 41(2), 221-225
CODEN: JHTCAD; ISSN: 0022-152X
PB HeteroCorporation
DT Journal
LA English
OS CASREACT 141:71518
AB A new heterocyclic bioreductive bis-alkylating agent, 2,3-bis(chloromethyl)benzo[g]quinoxaline-5,10-dione, was prepared in a four-steps synthesis. It was shown to react under electron transfer conditions with 2-nitropropane anion by an bis-SRN1 mechanism to give three C-alkylation products in excellent yields. Extension of this bis-SRN1 reaction to various nitronate or malonate anions and S-centered anions led to a new class of potentially active benzo[g]quinoxaline-5,10-dione derivs.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:306980 CAPLUS
DN 141:33320
TI Design, synthesis and biological activity of amidinobicyclic compounds (derivatives of DX-9065a) as factor Xa inhibitors: SAR study of S1 and aryl binding sites
AU Komoriya, Satoshi; Kanaya, Naoaki; Nagahara, Takayasu; Yokoyama, Asako; Inamura, Kazue; Yokoyama, Yukio; Katakura, Shin-ichi; Hara, Tsuyoshi
CS Tokyo R&D Center, Daiichi Pharmaceutical Co. Ltd, Edogawa-ku, Tokyo, 134-8630, Japan
SO Bioorganic & Medicinal Chemistry (2004), 12(9), 2099-2114
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Ltd.
DT Journal
LA English
OS CASREACT 141:33320
AB Since factor Xa (fXa) plays a pivotal role in the blood coagulation cascade, inhibition of fXa is thought to be an effective treatment for a variety of thrombotic events. (2S)-2-[4-[[(3S)-1-Acetimidoyl-3-pyrrolidinyl]oxy]phenyl]-3-(7-amidino-2-naphthyl)propanoic acid hydrochloride pentahydrate (DX-9065a) was previously found in our laboratory as a novel orally active factor Xa inhibitor. DX-9065a exhibits a strong inhibitory activity toward fXa by occupying the substrate recognition (called S1) sites and aryl binding sites of fXa. Herein we describe conversions of the amidinonaphthalene and the acetimidoylpyrrolidine moieties of DX-9065a. Some compds. showed remarkably increased in vitro anti-factor Xa and PRCT activities compared with those of DX-9065a. The most promising compound 38 showed four times the prolongation of APTT against DX-9065a after oral administration to rats.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:814483 CAPLUS
DN 140:263036
TI A New Double-Decker Lu(III) Diphthalocyanine with Eight Peripheral Benzo-15-crown-5 Units
AU Kocak, M. Burkut; Cihan, Ali; Guersoy, Sueleyman; Okur, A. Ihsan; Guel, Ahmet; Bekaroglu, Oezer
CS Department of Chemistry, Technical University of Istanbul, Istanbul, Turk.
SO Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry (2003), 33(9), 1527-1533
CODEN: SRIMCN; ISSN: 0094-5714
PB Marcel Dekker, Inc.
DT Journal
LA English
AB The authors describe a lutetium(III) bis(phthalocyaninate) complex which contains eight (benzo-15-crown-5)bis(ethoxycarbonyl)oxopropyl units. The starting compound was di-Et (3,4-dicyanophenyl)acetoxy(benzo-15-crown-5)malonate (1). The synthesis of the desired compound was accomplished by the reaction of 1 with lutetium acetate in hexanol in the presence of 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) as a strong base. The ESR spectrum confirmed the radical nature of the complex.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:644244 CAPLUS
DN 139:307656
TI A direct entry to the 1-methoxyindole skeleton and to the corresponding indoles by a novel rearrangement: general syntheses of substituted 1-methoxyindoles
AU Selvakumar, N.; Reddy, B. Yadi; Azhagan, A. Malar; Khera, Manoj Kumar; Babu, J. Moses; Iqbal, Javed
CS Department of Discovery Chemistry, Discovery Research, Dr. Reddy's Laboratories Ltd., Hyderabad, 500 050, India
SO Tetrahedron Letters (2003), 44(37), 7065-7069
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science B.V.
DT Journal
LA English
OS CASREACT 139:307656
GI

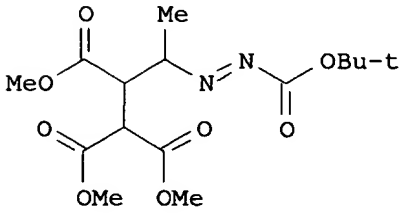


I

AB A short and efficient route to 1-methoxyindoles by a novel rearrangement is disclosed. This route involves only three steps from com. available nitro compds. The methodol. is also generalized with a variety of examples to afford a series of 2-substituted-1-methoxyindoles possessing an electron-withdrawing group at the 3-position. 1-Methoxyindole I (R = OMe) was converted to indole I (R = H) under mild conditions, thereby

constituting a new synthesis of substituted indoles.
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:93716 CAPLUS
DN 138:287593
TI Expeditious synthesis of new 1,2,3-thiadiazoles and 1,2,3-selenadiazoles from 1,2-diaza-1,3-butadienes via Hurd-Mori-type reactions
AU Attanasi, Orazio A.; De Crescentini, Lucia; Favi, Gianfranco; Filippone, Paolino; Giorgi, Gianluca; Mantellini, Fabio; Santeusanio, Stefania
CS Istituto di Chimica Organica, Universita degli Studi di Urbino, Urbino, 61029, Italy
SO Journal of Organic Chemistry (2003), 68(5), 1947-1953
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
OS CASREACT 138:287593
GI



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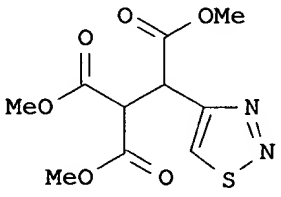

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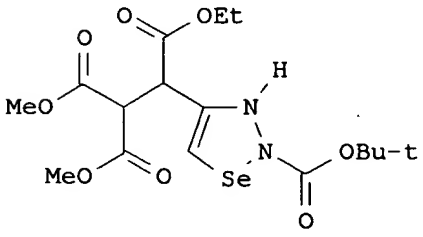

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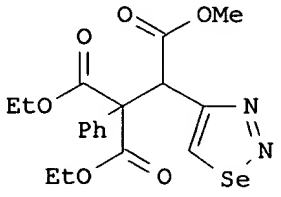


IV

AB α-Substituted hydrazones, e.g. I, obtained from 1,2-diaza-1,3-butadienes and methylenic or methinic activated substrates gave rise to a wide range of cyclic compds. In particular, in the presence of thionyl chloride as solvent-reagent, they were transformed into 1,2,3-thiadiazoles, e.g. II, with selenium oxychloride into new 4-substituted-2,3-dihydro-1,2,3-selenadiazoles, e.g. III, while with selenium dioxide, they were transformed into 4-substituted-1,2,3-selenadiazoles, e.g. IV. We have also examined the nucleophilic behavior of 1,2,3-thiadiazole II in the reaction with 1,2-diaza-1,3-butadienes that produced, under basic conditions, 4-hydrazono-1-(1,2,3-thiadiazolyl)pentane derivs. This event represents an interesting example of stereoselective synthesis because it leads exclusively to the formation of the RR/SS racemic mixture These latter compds., treated with thionyl chloride, gave the corresponding 1,3-di-1,2,3-thiadiazolylpropane derivs.,

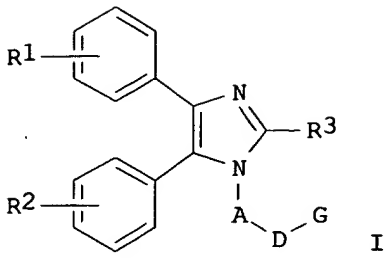
while with sodium methoxide they afforded 1,2,3-thiadiazolyl-2-oxo-2,3-dihydro-1H-pyrrole systems.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:849426 CAPLUS
DN 137:353021
TI Preparation of bisarylimidazolyl fatty acid amide hydrolase inhibitors for treatment of pain
IN Sit, Sing-Yuen; Xie, Kai
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002087569	A1	20021107	WO 2002-US12853	20020423
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002188009	A1	20021212	US 2002-128480	20020423
	US 6562846	B2	20030513		
	EP 1389107	A1	20040218	EP 2002-728952	20020423
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004532229	T2	20041021	JP 2002-584915	20020423
PRAI	US 2001-286827P	P	20010427		
	WO 2002-US12853	W	20020423		

OS MARPAT 137:353021
GI



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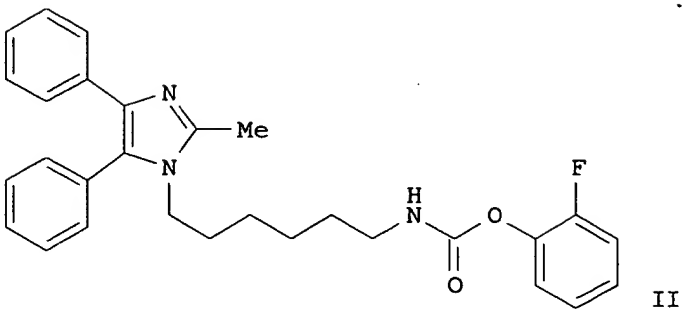


II

AB Title compds. I [wherein R1 and R2 = independently H, alkyl, or halo; R3 = (cyclo)alkyl; A = alkylene or L; L = C6H4O-alkylene; D = CO2, CONG1, NHCO2, or NHCO2N:CG1; G = H, haloalkyl, (cyclo)alkyl, pyridyl, or (un)substituted Ph or (CH2)1-2Ph; G1 = H or (halo)alkyl; or AD is optionally interrupted with CHJ, ZC6H4, or Z(CH2)1-3; Z = O or S; J = alkyl or Ph; with provisos] were prepared as fatty acid amide hydrolase (FAAH) inhibitors. For example, cycloaddn. of benzil with AcONH4 and MeCHO in glacial AcOH gave 2-methyl-4,5-diphenyl-1H-imidazole (29%). Alkylation with Et 7-bromoheptanoate in the presence of NaH in DMF (72%) followed by saponification with NaOH in EtOH afforded 7-(2-methyl-4,5-diphenylimidazol-1-yl)heptanoic acid. Stepwise addition of the azide, N3PO(OPh)2, and 2-FC6H4OH to a suspension of the heptanoic acid in TEA and toluene produced the carbamate II (55%). The latter inhibited recombinant human FAAH with IC50 < 10 nM. In addition, II gave results similar to known analgesics in the in vivo rat formalin test (acute and chronic chemo-induced pain assay), the Hargreaves test (acute thermal pain assay), and the Chung model (neuropathic pain assay). Thus, I and their pharmaceutical compns. are useful for the treatment of pain, particularly neuropathic pain, psychomotor disorder, hypertension, cardiovascular disease, eating disorder, nausea, AIDS-related complex, glaucoma, inflammation, psoriasis or multiple sclerosis, and other conditions the treatment of which can be effected by inhibiting FAAH.

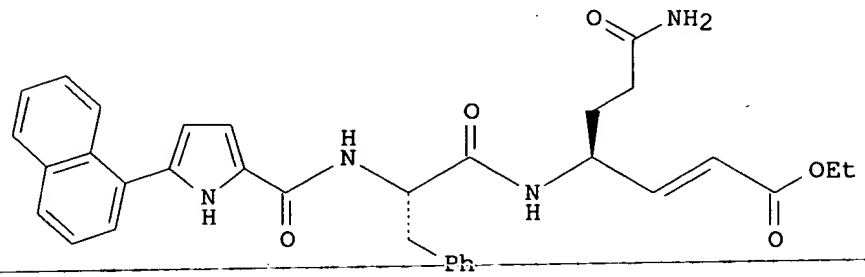
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:780850 CAPLUS
DN 135:331676
TI Preparation of pyrrole-containing peptidomimetic compounds as antipicornaviral agents
IN Johnson, Theodore O., Jr.; Hua, Ye; Luu, Hiep T.; Dragovich, Peter S.
PA Agouron Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 206 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079167	A2	20011025	WO 2001-US12333	20010412
	WO 2001079167	A3	20020228		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2406475	AA	20011025	CA 2001-2406475	20010412
	US 2002006943	A1	20020117	US 2001-834783	20010412
	US 6610730	B2	20030826		
	EP 1274682	A2	20030115	EP 2001-925037	20010412
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001010077	A	20030617	BR 2001-10077	20010412
	JP 2003531139	T2	20031021	JP 2001-576769	20010412
	ZA 2002008257	A	20030725	ZA 2002-8257	20021014
	US 2003225042	A1	20031204	US 2003-435082	20030512
PRAI	US 2000-197796P	P	20000414		
	US 2000-198497P	P	20000418		
	US 2001-834783	A3	20010412		
	WO 2001-US12333	W	20010412		

OS MARPAT 135:331676
GI



AB Peptidomimetic compds. RaCON(Rb)CHRcCRd:CZZ1 [Ra is alkyl-, cycloalkyl-, aryl- or heteroarylcarbonylalkyl, alkyl-, cycloalkyl-, heterocycloalkyl-, aryl- or heteroarylcarbonylaminoalkyl or -aminocarbonylalkyl, where each alkyl, cycloalkyl, heterocycloalkyl,aryl and heteroaryl may be substituted; Rb is H or (un)substituted alkyl; Rd is H, halo, OH, (un)substituted alkyl, alkoxy or alkylthio; Rc is CReRf-A1(R)-CO-A4-(A3)p-R, where R2 = (A2)m (m = 0 or 1; R = H for m = 0); Re, Rf = H, alkyl; p = 0-5; A1 = CH or N; A2 = CRgRhRi, NRgRi, SRg, S(O)Rg, SO2Rg, O(Rg) (Rg, Rh, Ri = H or alkyl); A3 = CRgRh, NRi, S, SO, SO2, O; A4 = NRjRk, CRgRhRi, O(Rk) (Rk = H or alkyl); Z, Z1 = H, F (un)substituted alkyl, cycloalkyl,

heterocycloalkyl, aryl or heteroaryl or CZZ1 is (hetero)cycloalkyl (with provisos)] were prepared for inhibiting or blocking the biol. activity of the picornaviral 3C protease. Thus, compound I was prepared by coupling 5-(1-naphthyl)-1H-pyrrole-2-carboxylic acid chloride (preparation given) with Phe-Gln-resin and showed Kobs/I = 30,800 M-1s-1 for inhibition of Rhinovirus 3C virus, EC50 = 0.109 μM in the anticoxsackieviral cell culture assay, and CC50 (50% cytotoxic dose) >10 μM.

L6 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:303088 CAPLUS
DN 135:122446
TI Straightforward entry to new 4-substituted 1,2,3-thiadiazoles from 1,2-diaza-1,3-butadienes via Hurd-Mori reaction
AU Attanasi, Orazio A.; De Crescentini, Lucia; Filippone, Paolino; Mantellini, Fabio
CS Istituto di Chimica Organica, Universita di Urbino, Urbino, 61029, Italy
SO Synlett (2001), (4), 557-559
CODEN: SYNLES; ISSN: 0936-5214
PB Georg Thieme Verlag
DT Journal
LA English
OS CASREACT 135:122446
AB 1-(Tert-butoxycarbonyl)-1,2-diaza-1,3-butadienes react with activated methylenic and methinic compds. to yield α-substituted hydrazones, which, in the presence of SOCl2 as solvent-reactant, led to 1,2,3-thiadiazoles via Hurd-Mori cyclocondensation.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:162869 CAPLUS
DN 134:347956
TI Design, syntheses, and structure-activity relationships of indan derivatives as endothelin antagonists; new lead generation of non-peptidic antagonist from peptidic leads
AU Morimoto, H.; Fukushima, C.; Yamauchi, R.; Hosino, T.; Kikkawa, K.; Yasuda, K.; Yamada, K.
CS Discovery Research Laboratory, Tanabe Seiyaku Co., Ltd, Toda-shi, Saitama, 335-8505, Japan
SO Bioorganic & Medicinal Chemistry (2001), 9(2), 255-268
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 134:347956
AB A new lead generation of non-peptidic ETA antagonists from two peptidic ETA-selective ones, BQ-123 and FR139317, was performed. Using computer assisted mol. modeling, a putative pharmacophore was constructed from the superposition of the reported three-dimensional structure of the cyclic peptide BQ-123 and a presumable β-turn active conformation of the linear peptide FR139317 formed by an intramol. hydrogen bond. According to this model, a new series of indan derivs. were designed and synthesized. Among these, 5-isobutyrylamino-6-(1-naphthylmethyloxy)-3-(2-thienyl)-1-indancarboxylic acid showed a moderate ETA antagonistic activity (IC50=28 μM).
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:152668 CAPLUS
DN 134:193420
TI Preparation of benzenepropanoic acid derivatives as fatty acid synthase inhibitors
IN Christensen, Siegfried B., IV; Daines, Robert A.; Leber, Jack D.; Weinstock, Joseph
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001014362	A1	20010301	WO 2000-US23073	20000823
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, DZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1206463	A1	20020522	EP 2000-957681	20000823
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003507467	T2	20030225	JP 2001-518449	20000823
PRAI	US 1999-150276P	P	19990823		
	WO 2000-US23073	W	20000823		

OS MARPAT 134:193420
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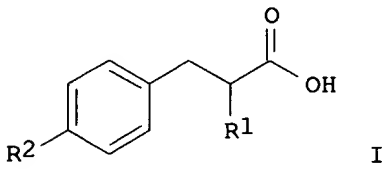

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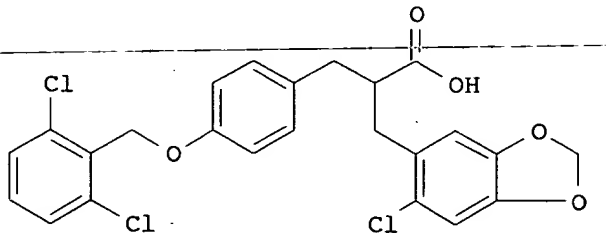


II

AB Title compds. (I) [wherein R1 = alkyl, (hetero)arylalkyl, heteroaryl, or (alkyl)cycloalkyl; R2 = O(CH2)mAr, NR3(CH2)mAr, NR4COAr, or NR4SO2Ar; R3 = H, alkyl(aryl), acyl, COAr; R4 = H or alkyl(aryl); Ar = (hetero)aryl; m = 0-3] were prepared as inhibitors of the fatty acid synthase, 3-ketoacyl-ACP

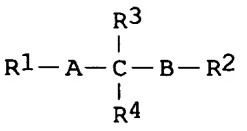
synthase (Fab H), for use as a new class of antibiotics. For example, the α-piperonylbenzenepropanoic acid (II) was formed by coupling 4-(2,6-dichlorobenzyloxy)benzaldehyde (preparation given) with di-Et malonate in the presence of piperidine and glacial AcOH in benzene (97%), reduction using NaBH4 in EtOH (88%), alkylation with 6-chloropiperonyl chloride in DMF (85%), and deesterification using KOH in EtOH (100%). I are active against a wide range of organisms, including both Gram-neg. organisms, e.g. Escherichia coli and Klebsiella pneumoniae, and Gram-pos. organisms, e.g. Staphylococcus aureus, Streptococcus pneunomiae, Enterococcus faecalis, and Enterococcus faecium, including isolates resistant to existing antibiotics (no data).

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:441757 CAPLUS
DN 133:73936
TI Preparation of substituted malonic acid esters as ion channel activating agents
IN Beyer, Jurgen; Jensen, Bo Skaaning; Strobaek, Dorte; Christophersen, Palle; Teuber, Lene
PA Neurosearch A/S, Den.
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000037422	A2	20000629	WO 1999-DK731	19991222
	WO 2000037422	A3	20000914		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1140784	A2	20011010	EP 1999-962125	19991222
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002533318	T2	20021008	JP 2000-589494	19991222
	US 2002169203	A1	20021114	US 2001-854694	20010515
PRAI	DK 1998-1722	A	19981222		
	DK 1999-403	A	19990323		
	DK 1999-660	A	19990512		
	WO 1999-DK731	W	19991222		

OS MARPAT 133:73936
GI



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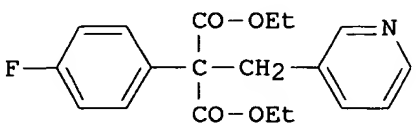

II

AB The invention relates to ion channel activating agents, specifically malonic acid esters (I) [wherein A and B = independently (CH2)n, (CH2)nY, Y(CH2)n, or (CH2)nY(CH2)m; m and n = independently 0-4; Y = O, S, or (alkyl)amino; R1, R2, R3, and R4 = independently (cyclo)alkyl, alkenyl, alkynyl, amino, trihalomethyl, NO2, CN, Ph, alkoxy(alkyl), alkylthio(alkyl), acyl, amido, carboxy, (un)substituted heterocyclyl or aryl(alkyl), etc.; or R3 and R4 together = (un)substituted polycyclic or hetero(poly)cyclic group]. In particular, the compds. are useful as openers SKCa, IKCa, and BKCa channels. The invention also relates to the use of these SK/IK/BK channel-activating agents for the manufacture of medicaments, and to pharmaceutical compns. comprising them. The compds. are useful for the treatment or alleviation of a wide variety of diseases and conditions associated with SK/IK/BK channels, including respiratory diseases such as asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic kidney disease, bladder spasms, urinary incontinence, bladder outflow obstruction, irritable bowel syndrome, gastrointestinal dysfunction, secretory diarrhea, ischemia, cerebral ischemia, ischemic heart disease, angina pectoris, coronary heart disease, traumatic brain injury, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, dysmenorrhea, narcolepsy, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, migraine, arrhythmia, hypertension, absence seizures, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labour, baldness, cancer, and immune suppression. In particular, the compds. are expected to be useful as immunosuppressants. For instance, addition of 3-picolyl chloride to di-Et 2-(4-fluorophenyl)malonate treated with NaH in DMF and heating to 80°C overnight gave II (22%). In an electrophysiol. experiment using cloned human placental intermediate-conductance Ca2+-activated K+ channels (IK channels), expressed in HEK293 cells, II and other invention compds. showed activity at concns. of ≤ 10 μM, and are thus potent SK/IK/BK channel activating agents.

L6 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:286739 CAPLUS
DN 133:98612
TI Novel crown ether-substituted phthalocyanines
AU Kocak, Makbule; Cihan, Ali; Okur, Ali Ihsan; Gul, Ahmet; Bekaroglu, Ozer
CS Department of Chemistry, Technical University of Istanbul, Istanbul, 80626, Turk.
SO Dyes and Pigments (2000), 45(1), 9-14
CODEN: DYPIDX; ISSN: 0143-7208
PB Elsevier Science Ltd.
DT Journal
LA English
AB A novel macrocycle was synthesized from 4'-(α-bromoacetyl)benzo-15-crown-5,4-nitrophthalonitrile and di-Et malonate; its cyclotetramerization gives Cu(II), Co(II) and Pd(II) phthalocyanines (Pcs) with four benzo-15-crown-5 substituents on the periphery. The effects of alkali metal cations with these Pcs was studied through the changes in the visible spectra. The newly synthesized compds. also were characterized by elemental analyses, IR, 1H NMR.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:210184 CAPLUS
DN 132:222660
TI Phosphonic acid derivatives as inhibitors of PTP-1B
IN Leblanc, Yves; Dufresne, Claude; Wang, Zhaoyin; Li, Chun Sing; Gauthier, Jacques Y.; Therien, Michel; Lau, Cheuk K.; Roy, Patrick
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000017211	A1	20000330	WO 1999-CA864	19990921
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6174874	B1	20010116	US 1999-398356	19990917
	CA 2344927	AA	20000330	CA 1999-2344927	19990921
	AU 9957241	A1	20000410	AU 1999-57241	19990921
	AU 761596	B2	20030605		
	EP 1115729	A1	20010718	EP 1999-944200	19990921
	EP 1115729	B1	20030219		
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	AT 232873	E	20030315	AT 1999-944200	19990921
	ES 2192396	T3	20031001	ES 1999-944200	19990921
PRAI	US 1998-101164P	P	19980921		
	US 1999-127420P	P	19990401		
	WO 1999-CA864	W	19990921		

OS MARPAT 132:222660
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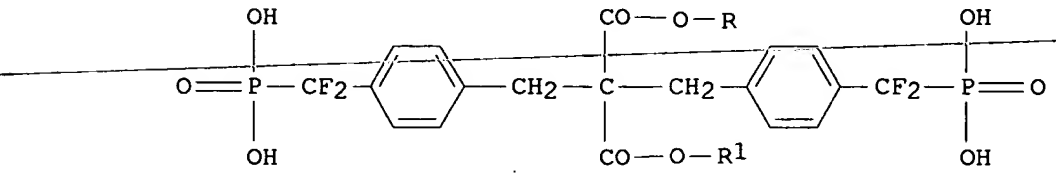


I

AB Anti-diabetic and anti-obesity title compds. such as malonates I (R = R1 = benzyl, I-Pr, H; R = Me, R1 = benzyl, H) were prepared by several standard methods. Among the approx. 50 compds. prepared were (4-{3-(benzyloxy)-2-(benzyloxycarbonyl)-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-oxopropyl}phenyl)difluoromethylphosphonic acid, (4-{3-(benzyloxy)-2-(benzyloxycarbonyl)-2-[4-(1,2,3-thiadiazol-4-yl)benzyl]-3-

oxopropyl}phenyl)difluoromethylphosphonic acid, bis{4-[difluoro(phosphono)methyl]benzyl}di-2-benzothiazolylmethane, and {4-[2-benzotriazol-1-yl-3-(4-bromophenyl)-2-phenylpropyl]phenyl}difluoromethylphosphonic acid.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

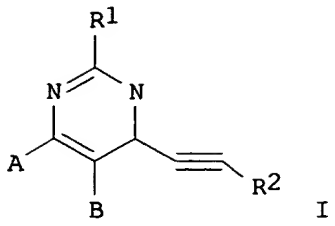
L6 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:196451 CAPLUS
DN 133:26469
TI AMP Deaminase Inhibitors. 4. Further N3-Substituted Coformycin Aglycon Analogs: N3-Alkylmalonates as Ribose 5'-Monophosphate Mimetics
AU Bookser, Brett C.; Kasibhatla, Srinivas Rao; Erion, Mark D.
CS Metabasis Therapeutics Inc., San Diego, CA, 92121, USA
SO Journal of Medicinal Chemistry (2000), 43(8), 1519-1524
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB AMP deaminase (AMPDA) inhibitors increase the levels of extracellular adenosine and preserve intracellular adenylate pools in cellular models of ATP depletion and therefore represent a potential new class of antiischemic drugs. Recently we reported that replacement of the ribose 5'-monophosphate component of the very potent transition-state analog AMPDA inhibitor coformycin monophosphate with a simple alkylcarboxy group resulted in potent, selective, and cell-penetrating AMPDA inhibitors. Here we report that replacement of this alkylcarboxy group with an α-substituted alkylmalonic acid resulted in enhanced inhibitor potency. The lead compound, 3-(5,5-dicarboxy-6-(3-(trifluoromethyl)phenyl)-n-hexyl)coformycin aglycon, exhibited an AMPDA Ki of 0.029 μM which is (3 + 105)-fold lower than the KM for the natural substrate AMP. A comparison of inhibitory potencies shows that the diacid analogs with α-benzyl substituents are 2-10-fold more inhibitory than similar monoacid-monoester, monoester-monoamide, or diester derivs. Finally, these diacid analogs are 2-40-fold more potent inhibitors than the corresponding monocarboxylates.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:206884 CAPLUS
DN 130:267450
TI Preparation of ethynylpyrimidine derivatives as tyrosine kinase inhibitors and their pharmaceutical uses
IN Kitano, Yasunori; Kawahara, Eiji; Takayanagi, Hisao; Suzuki, Takeshi; Ohya, Atsushi; Hara, Hiroto
PA Mitsubishi Chemical Industries Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 235 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 11080131	A2	19990326	JP 1997-251348	19970901
PRAI JP 1997-251348		19970901		

OS MARPAT 130:267450
GI



I

AB The derivs. I [A, B = NO2, (CH2)n (n = 0, 1), NR3R4 (R3, R4 = H, C1-5 alkyl which may be substituted with CO2H or C1-5 alkoxycarbonyl) or AB = CX1:CX2CX3:CX4 [X1-X4 = H, halo, NO2, OR (R = C3-8 cycloalkyl which may contain O, C1-5 alkyl which may be substituted with C1-5 alkoxy, amino, morpholino), amino which may be substituted with C1-5 alkyl; neighboring 2 groups of X1-X4 may be bonded to each other to be C1-5 oxyalkylene], N:CX5CX6:CX7 (X5-X7 = H, halo, C1-5 alkoxy, amino which may be substituted with C1-5 alkyl), CX8:NCX9:CX10 (X8-X10 = any group given for X5-X7), N:CX11CX12:N (X11, X12 = H, C1-5 alkyl), W:CX13NX14 (W = N, CX15, X13-X15 = H, C1-5 alkyl), CX16:CX17O (X15, X17 = H, C1-5 alkyl); R1 = H, halo, (halo)phenyl, C1-5 (phenyl)alkyl, C1-5 alkoxy which may be substituted with CO2H or C1-5 alkoxycarbonyl, OH, amino which may be substituted with C1-5 alkyl or C1-5 alkanoyl; R2 = CR3R4R5 [R3, R4 = H, halo, pyridyl, pyridazinyl, (C3-8 cycloalkyl)-C1-5 alkyl, etc.]; R5 = OH, C1-5 alkyl, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, CO2H, etc], their hydrates, pharmacol. acceptable salts, optically-active isomers, racemates, and diastereomer mixts. are prepared I are useful for prophylactic and/or therapeutic agents for diseases due to acceleration of tyrosine kinase activity, e.g. as antitumor agents, immunosuppressants, platelet aggregation inhibitors, antiatherosclerotics, inflammation inhibitors, etc. Et2NCMe2C.tplbond.CH was treated with EtMgBr and the resulting grignard reagent was treated with 4-chloro-2-phenylquinazoline (preparation given) to give I (R1 = Ph, R2 = CMe2NEt2, AB = CH:CHCH:CH) (II). This was dissolved in Et2O and treated with HCl/EtOAc to give II.HCl. IC50 values of this salt against EGF receptor tyrosine kinase activity and growth of human nasopharyngeal carcinoma KB cells were 14 μM and 0.89 μM, resp.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	438.55	600.09

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-70.08	-70.08

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